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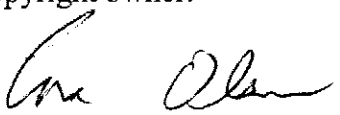

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ABSTRACT

Syndromic Surveillance and Outbreak Detection Using Automated Microbiologic Laboratory Test Order Data

Cara Hendricks Olsen

Doctor of Public Health Degree, 2007

Thesis directed by David F. Cruess, PhD, Department of Preventive Medicine and Biometrics

Background: Syndromic surveillance systems monitor one or more electronic data sources in real time to assist in early detection of unusual health events. To detect such events at military treatment facilities (MTFs), the Department of Defense Electronic Surveillance System for the Early Notification of Community-based Epidemics (DoD-ESSENCE) conducts daily surveillance on outpatient visit diagnosis and pharmacy data. Combining data from multiple sources may improve the ability of syndromic surveillance systems to detect disease outbreaks.

Objective: To evaluate whether data on microbiologic laboratory tests ordered for patients during outpatient visits to MTFs can improve the performance of DoD-ESSENCE in detecting disease outbreaks.

Specific Aims:

(1) Identify microbiology laboratory tests for which frequency of ordering increases during disease outbreaks, and frequency of ordering follows similar patterns to frequency of outpatient visits for disease syndromes monitored by DoD-ESSENCE.

(2) Evaluate and compare strategies for using test orders for syndromic surveillance, alone and in combination with outpatient visit data.

Study Design: Secondary analysis of electronic medical records database.

Relevance: Early and reliable detection and intervention can reduce the consequences of disease outbreaks.

Results: Related laboratory test orders can be combined into syndromes that align closely both with existing surveillance using outpatient data, and with CDC expert panel recommendations. Sensitivity, specificity, and timeliness of surveillance using laboratory-based respiratory and gastrointestinal syndrome data are similar to surveillance using outpatient visit data. Combining the data sources may lead to increased timeliness of outbreak detection and improve the performance of DoD-ESSENCE.

Conclusion: Data on laboratory test orders, currently collected and archived for administrative purposes, may be useful as a supplementary data source for syndromic surveillance.

SYNDROMIC SURVEILLANCE AND OUTBREAK DETECTION USING AUTOMATED MICROBIOLOGIC LABORATORY TEST ORDER DATA

by

Cara Hendricks Olsen

Dissertation submitted to the Faculty of the
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List of Abbreviations

AFB	acid-fast bacilli
ARMA	autoregressive moving average
CDC	Centers for Disease Control and Prevention
CHCS	Composite Health Care System
CSF	cerebrospinal fluid
CUSUM	cumulative sum
DARPA	Defense Advanced Research Projects Agency
DoD	Department of Defense
DOHMH	Department of Health and Mental Hygiene
EARS	Early Aberration Reporting System
EI/DS	Executive Information / Decision Support
ESSENCE	Electronic Surveillance System for the Early Notification of Community-based Epidemics
EWMA	exponentially weighted moving average
GI	gastrointestinal
HL7	health level 7
ICD9	International Classification of Diseases, 9th revision
JHU/APL	Johns Hopkins University Applied Physics Lab
LOINC	Logical Observation Identifiers Names and Codes
MEWMA	multivariate exponentially weighted moving average
MRSA	Methicillin-resistant *Staphylococcus Aureus*
MTF	military treatment facility
NCA	national capital area
PH	public health
ROC	receiver-operating characteristic
RODS	Real-time Outbreak Detection System
SADR	Standard Ambulatory Data Record
SD	standard deviation
SNOMED	Systematized Nomenclature of Medicine
SNR	signal-to-noise ratio
USUHS	Uniformed Services University of the Health Sciences
WRAIR	Walter Reed Army Institute of Research

CHAPTER I: Introduction

Syndromic surveillance systems monitor one or more electronic data sources in real time to assist in early detection of unusual health events. To detect such events at military treatment facilities (MTFs), the Department of Defense Electronic Surveillance System for the Early Notification of Community-based Epidemics (DoD-ESSENCE) conducts daily surveillance on outpatient visit diagnosis and pharmacy data. Combining data from multiple sources may improve the ability of syndromic surveillance systems to detect disease outbreaks.

The purpose of this study is to evaluate whether data on microbiologic and serologic laboratory tests ordered for patients by providers during outpatient visits to military treatment facilities (MTFs) can improve the performance of DoD-ESSENCE in detecting disease outbreaks. Improved performance will be measured by sensitivity, specificity and timeliness of outbreak detection. This chapter will describe the specific aims and public health significance of the study.

Specific Aims

The first specific aim is to identify laboratory tests that may be associated with disease outbreaks, and with other measures of disease prevalence. We will identify laboratory tests that meet the criteria outlined below:

- The laboratory test is more likely to be ordered during an outpatient visit in which the patient is diagnosed with a disease syndrome under surveillance by ESSENCE, than during an outpatient visit in which no such syndrome is diagnosed.

- Daily counts of the laboratory test are positively correlated over time with daily counts of outpatient visits for one or more of the disease syndromes under surveillance by ESSENCE.
- Daily counts of the laboratory test are higher during outbreaks of a disease syndrome under surveillance by DoD-ESSENCE than during non-outbreak periods.

We will propose individual laboratory tests, or syndrome groupings comprised of several related laboratory tests, for surveillance

The second specific aim is to develop and compare several strategies for using laboratory test orders for syndromic surveillance, alone and in combination with outpatient visit data. Surveillance strategies will be developed for one or more laboratory tests or syndromes identified under the first specific aim. Components of the second specific aim include:

- Identify appropriate statistical model(s) for estimating the expected daily number of laboratory tests, based on the distribution of the observed data.
- Identify and implement one or more methods for combining laboratory test order data with outpatient visit data for surveillance.
- Compare these models and methods with respect to timeliness, sensitivity, and specificity of outbreak detection, and identify the most promising strategy.

Public Health Significance

The stated goal of this project is to improve the performance of a syndromic surveillance system for early detection of outbreaks. The public health significance of the project, therefore, is contingent upon the importance of early outbreak detection in

protecting public health, and the potential of the data to improve early detection. This section will summarize these two points, and discuss expected conclusions of the study.

In theory, early detection of outbreaks is important because it gives public health officials time to intervene to prevent the spread of disease and reduce morbidity and mortality. Early detection of disease is only useful if an intervention exists that, if administered early, can reduce morbidity and mortality. The course of many infectious diseases includes a nonspecific prodrome in which symptoms of the disease may be confused with other diseases, and during which intervention may save the life of the patient. Anthrax, for example, has a prodrome lasting from several hours to several days [1], and administering antibiotics during this period can protect against the fatal consequences of the fully-developed disease. While the relatively short prodrome increases the likelihood that the first case will be identified by a clinician before syndromic surveillance triggers an investigation [1], syndromic surveillance can be used to discern the size and geographic spread of the outbreak and identify potential cases. Smallpox has a prodrome lasting 7 to 19 days, and administration of the smallpox vaccine during the first four days after exposure is protective [2]. An effective syndromic surveillance system can be an important tool for public health officers and can trigger early investigations and interventions to both minimize disease severity and to halt further person-to-person transmission.

Since the anthrax attacks of 2001, several articles have been written about the importance of early intervention. Brookmeyer and Blades [3] estimated that in the absence of antibiotic prophylaxis, the number of deaths resulting from the anthrax attacks would have doubled. An economic model developed by Kaufmann et al [4] showed that

the single most important means of reducing losses after an anthrax, tularemia, or brucellosis attack is post attack prophylaxis, and that the earlier the prophylaxis program is initiated, the greater the savings.

The earlier an outbreak is detected, the earlier public health interventions can be initiated. Wagner et al. [5] outline four methods for improving timeliness of detection: (1) improving the quality of existing data sources, (2) adding new data sources, (3) improving the detection algorithm, and (4) reducing the specificity of the detection algorithm. The reason that adding new data sources can improve timeliness is that it can reinforce the outbreak "signal" relative to the "noise" in the data. The result is analogous to increasing the sample size.

We expect to show that laboratory test orders may be combined into syndrome groups similar to those proposed by the CDC, and that these syndrome groups will correlate well with ICD-9 based syndromes for outpatient visit data. The syndrome groups may be used by others, and the classification algorithm developed during this study may be used as a starting point for a free-text classification algorithm for prospective data collection.

We also anticipate that combined surveillance using both laboratory test orders and outpatient visit data will show better performance in the outbreak detection evaluation than surveillance using either data set alone. In this way, the results of the study can be used to improve the timeliness of outbreak detection, increasing the likelihood of early intervention.

CHAPTER II: Background and Significance

This section will discuss syndromic surveillance, place it within the context of disease surveillance in general, and discuss important aspects of syndromic surveillance including data sources, case definitions, algorithms, and evaluation methods used for syndromic surveillance.

Syndromic surveillance

Syndromic surveillance systems have been developed as a way to reduce the consequences of disease outbreaks through early detection and intervention. Generally, these systems monitor health-related events that precede diagnosis, such as visits to a primary care provider or emergency department, or medication prescriptions. An unexpected increase in these events triggers an alert and subsequent outbreak investigation. Syndromic surveillance can trigger an investigation earlier in the course of the disease outbreak than traditional, diagnosis-based surveillance. Earlier investigation can lead to earlier public health interventions, including (1) identifying and containing the source of the outbreak, (2) working to prevent illness in exposed persons, and (3) identifying and treating cases of disease early in their course, thus saving lives and resources.

No uniform definition of syndromic surveillance has been adopted. We list five representative definitions from the syndromic surveillance literature:

- A spectrum of activities that include monitoring illness syndromes or events, such as medication purchases, that reflect the prodromes of bioterrorism-related diseases [1].

- The surveillance of disease syndromes (groups of signs and symptoms), rather than specific, clinical, or laboratory-defined diseases [6].
- An investigational approach where health department staff, assisted by automated data acquisition and generation of statistical alerts, monitor disease indicators in real-time or near real-time to detect outbreaks of disease earlier than would otherwise be possible with traditional public health methods [7].
- The monitoring of available data sources for outbreaks of unspecified disease or of specified disease before identifying symptoms are confirmed [8].
- The ongoing, systematic collection, analysis and interpretation, and application of real-time (or near-real-time) indicators for diseases and outbreaks that allow for their detection before public health authorities would otherwise note them. Syndromic surveillance is distinguished from other methods of surveillance by the data types that are monitored as potential indicators of a disease or outbreak [9].

Each of these definitions emphasizes one or more important aspects of syndromic surveillance: data sources (automated electronic data), case definitions (groups of signs and symptoms rather than laboratory-based diagnoses), and outcomes (statistical alerts that may signal disease outbreaks). These aspects will be discussed in detail below.

The goal of syndromic surveillance has been defined as "to enable earlier detection of epidemics and a more timely public health response, hours or days before disease clusters are recognized clinically, or before specific diagnoses are made and reported to public health authorities" [1], or according to Burkom et al. [8], "To complement existing sentinel surveillance by identifying outbreaks with false-alert rates

acceptable to the public health infrastructure." A high priority for syndromic surveillance systems is early detection of outbreaks. However, practical experience has shown that syndromic surveillance may also be useful for estimating the magnitude of a health problem, documenting the distribution and spread of a health event, evaluating control and prevention measures, and detecting changes in health practice. For example, during the SARS outbreak of 2003, syndromic surveillance was used to reassure public health officials that the disease was not widespread in the United States [10]. After former President Clinton's cardiac bypass surgery in September 2004, syndromic surveillance systems documented a change in patient behavior, as indicated by an increase in patients seeking care for chest pain [11]. Montgomery County, Maryland used syndromic surveillance to determine when to begin and end an influenza vaccination program [12]. Finally, when outbreaks are detected, either through syndromic surveillance or traditional methods, the electronic data used for syndromic surveillance can be used to identify and locate patients with signs and symptoms of the illness, so that they can be interviewed and tested during an epidemiologic investigation.

Syndromic surveillance has been effective at detecting naturally occurring outbreaks such as food-borne or water-borne outbreaks of gastrointestinal disease, and seasonal outbreaks of respiratory disease [13]. It also appears promising for detection of disease outbreaks due to bioterrorist attacks, although its true effectiveness cannot be determined in the absence of such an attack. In addition, even if an outbreak is first detected by other means, syndromic surveillance provides a mechanism for monitoring the outbreak in near-real time that does not add to the burden of healthcare providers.

One of the earliest examples of a syndromic surveillance system is ESSENCE, the Electronic Surveillance System for the Early Notification of Community-based Epidemics. Researchers at the Walter Reed Army Institute of Research (WRAIR) developed ESSENCE initially to detect infectious disease outbreaks at military treatment facilities in the National Capital Area. Following the events of September 11, 2001, surveillance was expanded to cover active duty personnel and beneficiaries at more than 300 military treatment facilities worldwide. ESSENCE monitors outpatient visits by grouping International Classification of Diseases, 9th Revision (ICD-9) diagnostic codes into syndrome groups. Baseline levels of outpatient visits in these groups have been established, and fluctuations are monitored on a daily basis. When a significant increase is detected, an outbreak investigation may be initiated. A related system, ESSENCE II, was developed in collaboration with the Johns Hopkins University Applied Physics Lab, and monitors both civilian and military data sources in the Washington, D.C. region. ESSENCE II is described in detail in Lombardo et al. [12]. This study deals exclusively with the military version of ESSENCE, referred to below as "DoD-ESSENCE".

Syndromic surveillance has several important limitations. First, it may only be useful for detecting particular sizes and types of outbreaks. Buehler et al. [1] suggest that syndromic surveillance is most likely to detect an outbreak earlier than it would be detected by clinical reporting if the distribution of the incubation period is narrow, the disease has a long prodrome, there is an absence of specific clinical signs during the prodrome, and diagnosis is unlikely during routine care. Anthrax, because of its variable incubation period and relatively short prodrome, is likely to be detected clinically before enough cases occur to trigger an alert through syndromic surveillance. Smallpox, on the

other hand, has a long, nonspecific early phase that may be detected by syndromic surveillance. There is no way to predict whether naturally-occurring emerging infections, or known agents modified by bioterrorists, would have characteristics that would lead to early detection through syndromic surveillance. Syndromic surveillance is a useful adjunct to, not a replacement for, clinician reporting and other traditional surveillance methods.

A second limitation is the inherent tradeoff among sensitivity, specificity, and timeliness. Early syndromic surveillance systems were prone to frequent false alarms. Systems may be designed to improve specificity (and reduce false alarms) by setting a higher threshold for alerts, but this reduces their ability to detect real outbreaks, and to detect them early [14]. The only way to improve one aspect of performance without decreasing other aspects of performance is to change the system, possibly by adding new data sources or improving detection algorithms.

Finally, the output of a syndromic surveillance system is a statistical alert. In order for syndromic surveillance to have any effect on public health, it must be integrated with the public health response system so that an epidemiologic investigation and appropriate public health response can take place. While Stoto et al. consider this a limitation of syndromic surveillance, it is in fact a characteristic of all surveillance systems. It is critical, however, that syndromic surveillance systems be designed for ease of use by public health practitioners, so that system use, and public health benefits, can be maximized.

Disease surveillance

Public health surveillance has been defined as the "ongoing, systematic collection, analysis and interpretation of health data essential to the planning, implementation, and evaluation of public health practice, closely integrated with the timely dissemination of these data to those who need to know. The final link of the surveillance chain is the application of these data to prevention and control. A surveillance system includes a functional capacity for data collection, analysis, and dissemination linked to public health programs"[15]. Within this definition, different approaches to public health surveillance are distinguished by their goals, uses and data sources. Syndromic surveillance focuses specifically on early detection of outbreaks, but as discussed above, may be useful for other purposes as well.

Parrish and McDonnell [16] divide data collection activities for surveillance into two categories: primary and secondary. Primary data collection includes interviews, such as completion of a death certificate after speaking with the deceased's next-of-kin; and observation, such as the physical exam portion of the National Health and Nutrition Examination Study. These methods are costly and time consuming for both the participant and the interviewer/examiner. Secondary data collection, on the other hand, involves existing records or data collected for another purpose, such as records review. Secondary data collection is generally faster and less expensive than primary data collection, but since the data were not specifically collected for surveillance, the quality is likely to be lower. Syndromic surveillance is an example of secondary data collection. Since timeliness is critical for outbreak detection, the lower quality of the data is accepted as a necessary trade-off for faster data collection.

Surveillance systems are often classified into active and passive systems. Active systems require public health personnel to seek out cases by contacting health care providers, while passive systems rely on health care providers to send reports periodically to health departments [17]. Syndromic surveillance, however, combines the ease of passive surveillance with the capture of active surveillance. Syndromic surveillance typically uses records that are already collected for other purposes such as billing or medical records. An automated electronic transfer system is usually set up so that neither the health care provider nor public health personnel must actively seek cases. Public health personnel are typically responsible for monitoring syndromic surveillance data over time.

Electronic data sources

Syndromic surveillance "gathers information about the group of symptoms experienced by cases during the early phase of illness" [6]. Information on these symptoms may be obtained directly from clinical information, or indirectly from surrogate data sources. Clinical information sources commonly used for syndromic surveillance include emergency department chief complaints, hospital admissions, outpatient diagnoses, pharmacy prescriptions, 911 calls, and nurse hotline calls [6, 18]. Various systems incorporate non-clinical data, such as school or work absenteeism and over-the-counter medication sales, as well [12, 19].

Syndromic surveillance systems rely on electronic data sources for several reasons. First is the importance of timeliness in outbreak detection. Electronic data can be transmitted and analyzed more quickly than traditional pencil-and-paper or phone reporting. For example, Mostashari et al. [20] showed that annual influenza outbreaks in

New York City are typically detected two to three weeks earlier by syndromic surveillance based on ambulance dispatch calls than by traditional sentinel physician surveillance. The fact that syndromic surveillance using electronic data uses data that are already generated for other purposes means that it does not add to the burden of providers, either in time or cost. The timeliness of electronic data, however, depends on how quickly providers enter and transmit the data. In DoD-ESSENCE, for example, most of the outpatient data is available for surveillance within one to three days of a patient encounter [21]. Immediate data entry, transmission, and analysis would improve the timeliness of outbreak detection.

Laboratory test order data is a promising data source for improving syndromic surveillance that has been recommended by several authors [6, 7]. Pavlin et al. [22] point out that while laboratory tests are ordered by clinicians and may reflect actual illness patterns, tests are not ordered for all (or most) patients, so may not provide as complete a picture of disease patterns as other data sources. However, laboratory tests may complement other data sources in important ways. Since laboratory tests may be ordered for the sickest patients, surveillance of laboratory test data may be more specific for severe disease. When a diagnosis cannot be made at the initial visit, the types of tests ordered may provide more information about the patient's symptoms than is provided by other information contained in electronic records, such as ICD-9 diagnostic codes. Surveillance conducted on laboratory tests as they are ordered, rather than as the results are obtained, may give an early indication of disease outbreaks.

No other study has examined the use of laboratory test orders for syndromic surveillance. Although laboratory test order data have been proposed as a data source by

several authors, such data are not widely available. The CDC began receiving data in 2004 from a civilian laboratory, LabCorp®, which conducts laboratory tests nationwide. Although the CDC has proposed syndrome definitions and has begun conducting surveillance on laboratory test orders [23], they have not conducted an evaluation to validate the syndrome definitions or to determine whether laboratory test orders contribute to the detection of outbreaks. In addition, their data and target population are different from those considered in this study.

A few studies have used electronic laboratory test results for surveillance. Effler et al. [24] showed that electronic laboratory reports are more timely and complete than conventional reports, and a review by Bravata et al. [25] indicated that automated laboratory test results detect 76 – 100% of illness identified by traditional reporting methods. Koski et al. [26] showed that data from a commercial lab (the Quest Diagnostics data archive) could be used for influenza surveillance. Ma et al. [27] showed that seasonal and geographic patterns of West Nile Virus were well-represented in laboratory test order data. Hutwagner et al. [28] published one of the earliest studies of electronic surveillance, showing that electronic laboratory reports of *Salmonella* isolates were reasonably sensitive and specific for detecting *Salmonella* outbreaks, and were instrumental in early detection of an international *Salmonella* outbreak spread by contaminated alfalfa seeds in 1995.

Wagner et al., in a report commissioned by the Agency for Healthcare Research and Quality (AHRQ), suggested that data from clinical laboratory systems would be a good data source for surveillance because most laboratories are highly automated and report results electronically [29] . Unfortunately, DoD laboratory test results are not

reported in a standardized form and are not likely to available quickly enough to provide early indication of disease outbreaks, so they will not be considered in this study.

Only one published research study to date has analyzed DoD laboratory test data. Riegodedios et al. [30] combined laboratory test data with inpatient and outpatient visit records for patients diagnosed with one of four reportable diseases (malaria, syphilis, acute hepatitis B, and Lyme disease) to determine how many of these patients had a confirmatory laboratory test result. Overall, they found that only 19 percent of patients with an inpatient diagnosis code corresponding to one of these diseases, and only 16 percent of patients with an outpatient diagnosis code corresponding to one of these diseases, had a confirmatory laboratory test result. The study concluded that monitoring of inpatient and outpatient visit records alone would produce many false positive reports. An unpublished presentation [31] showed that DoD laboratory tests may be used to "track antibiotic resistance and antibiotic resistant infections, provide an initial and rapid analysis of medical event concerns, initiate epidemiologic investigations as needed, and generate hypotheses for further study." DoD laboratory data have proven useful for surveillance of specific pathogens, including group a beta-hemolytic *Streptococcus pyogenes*, methycillin-resistant *Staphylococcus aureus* (MRSA), and *Acinetobacter baumannii [32-34]*. This study complements the ongoing research by Riegodedios et al. by focusing specifically on syndromic surveillance.

Case definition and syndrome grouping

Syndromic surveillance typically monitors syndromes, not specific illnesses. These syndromes are defined by signs and symptoms rather than by laboratory-confirmed diagnoses. Monitoring syndromes can lead to earlier outbreak detection for two reasons:

first, many illnesses have similar signs and symptoms during early stages of illness, so syndromes can be recognized earlier than specific diseases; and second, laboratory confirmation of diagnoses can take a week or more.

DoD-ESSENCE currently monitors the following syndromes: botulism-like, fever, gastrointestinal, hemorrhagic, neurologic, rash, respiratory, and shock-coma. Syndromes are defined on the basis of ICD-9 diagnostic codes assigned to patients during outpatient visits to MTFs. Detailed definitions of the DoD-ESSENCE syndromes are in Appendix 3. These syndrome definitions were confirmed against the gold standard of physician chart review. Across three syndromes (respiratory, gastrointestinal and fever) and three hospital emergency departments, sensitivities ranged from 67-95% and specificities ranged from 92-97% [13].

The CDC convened a working group in 2004 to develop a preliminary assignment of laboratory tests to syndrome categories similar to those used by ESSENCE. A group of clinicians involved with syndromic surveillance were given a list of the laboratory tests for which the CDC obtains LabCorp data, and asked to assign each laboratory test to one or more syndromes. The committee compiled the assignments into a single list, discussed and resolved disagreements, and presented a preliminary grouping of laboratory tests into syndromes at the 2004 Syndromic Surveillance Conference [35]. The grouping is presented in Appendix 1, and is used as a reference for classifying laboratory tests in the DoD data set.

Once syndromes are defined, the next step is to develop a rule for assigning individual data records to syndrome groups. Unlike numeric ICD-9 codes, laboratory test orders are recorded as text in the DoD's electronic database. When categorizing free text

fields, it is important to account for the different terms, spellings, and abbreviations used by different providers and data entry personnel. Two basic approaches to text coding have been applied to syndromic surveillance: Bayesian classification and keyword classification. The Real-Time Outbreak Detection System (RODS) laboratory at the University of Pittsburgh has developed a Bayesian classification algorithm for assigning emergency department chief complaints to syndromes [36]. The first step in developing this algorithm was to produce a "training set" of nearly 30,000 chief complaint entries that were manually assigned to syndromes by a physician. The algorithm reads new chief complaint entries, compares them with the entries in the training set, and determines the probability that the new entry will fall into each syndrome, based on its similarity to entries in the training set and the syndromes to which the training set entries are assigned. The new entry is assigned to the syndrome with the highest probability.

The New York City Department of Health and Mental Hygeine (DOHMH) uses a different approach to classifying emergency department chief complaints [37]. Their system searches for keywords in each chief complaint entry, and if one or more keywords assigned to a syndrome are present in the entry, the entry is assigned to that syndrome. A recent study showed that the two methods had a moderate level of agreement (kappa = 0.614) when used to categorize the same data [38]. The civilian version of ESSENCE uses a form of keyword matching that is described by Sniegoski [39].

Both methods, however, are likely to misclassify some cases with unique spellings or abbreviations. Ideally, all laboratory tests could be classified by hand. In this study, because we will be analyzing a finite, retrospective data set, and because many laboratory test names (e.g., THROAT CUL) are used repeatedly, we can classify

laboratory test orders by hand. The classification we develop may be useful in the future to identify keywords for a classifier similar to the one used by the New York City DOHMH, or to use as a training set for a Bayesian classifier similar to the one used by RODS.

Algorithms for alerting

Syndromic surveillance systems generally monitor daily counts of health-related events over time and look for aberrations. Algorithms for aberration detection include three steps: (1) Estimate the expected count, (2) Compare the expected count with the observed count, (3) Signal an alert if the observed count is significantly larger than the expected count. An alert, however, does not signify that a disease outbreak has necessarily occurred, only that an unusual pattern has been observed in the data. An investigation is required to determine the cause of the unusual pattern.

Expected daily counts are estimated from recent data using methods from several different disciplines, including statistics, quality control, and epidemiology. Most statistical approaches are regression models of the basic form:

$$Y_t = X_t\beta + \varepsilon_t$$

where Y_t is the observed count at time t, X_t is a vector of characteristics of the current time period, β is a vector of regression coefficients, and ε_t is an independent and identically distributed error term. The X_t vector often includes such characteristics as season and day of the week, to account for cyclical patterns in the data. If counts are large, ε_t may be assumed to follow a normal distribution [40]. However, it is likely that the ε_ts are not independent because of serial correlation in the data. Standard time series regression models may be used in this situation. Reis et al. [41], for example, proposed

an autoregressive moving average (ARMA) model, in which the expected count in the current time period is estimated as the weighted sum of previous counts and previous residuals (differences between previous observed and expected counts).

If the counts are small, it may be unreasonable to assume normally distributed residuals, and Poisson regression may be more appropriate than linear regression. If counts are sufficiently small, even sporadic, serial correlation is not an issue [40]. Kleinman et al. [42] propose using generalized linear mixed models, of which Poisson regression is a subset, for surveillance, and in fact Poisson regression is used for syndromic surveillance in the Boston region [43].

One potential drawback of regression methods is that they require a substantial amount of historical data for model estimation and prediction. The CDC recommends at least three years of historical data if seasonal trends are to be estimated [44]. Most syndromic surveillance systems began after September 2001 and have limited historical data. In addition, automating regression models to monitor a variety of syndromes and data sources is problematic because the models often require fine tuning to achieve a good fit to the data [40].

Quality control methods, on the other hand, typically require only recent data for prediction. These methods have been adapted from manufacturing, where they are used to ensure that manufacturing processes stay within specified limits. Two such methods, exponentially weighted moving average (EWMA) and cumulative sums (CUSUM) are used in syndromic surveillance.

EWMA, also known as exponential smoothing, was first applied to monitoring surveillance data by Ngo et al. [45] for detecting nosocomial outbreaks. The predicted

count at the current time period is a weighted average of counts at previous time periods, with greater weights given to more recent time periods. The general formula is

$$\hat{y}_{t+1} = \alpha y_t + (1- \alpha)\, \hat{y}_t$$

where the parameter α is chosen to minimize the forecast error variance, $y_t - \hat{y}_t$.

EWMA is appropriate for independent and identically distributed data series. If there is a secular trend or a seasonal pattern, two adjacent time points are likely to have more similar counts than two distant time points. Some days, such as weekends and holidays, are likely to have lower average values because clinics are closed or fewer appointments are available on those days. These systematic changes in the data series over time can seriously affect the accuracy of forecasts [40]. However, if systematic differences in the mean can be removed by regression, EWMA may be used to monitor changes in the residuals.

CUSUM methods add up the deviations between observed and expected values over time. The CUSUM following time t is

$$S_t = \max(0, S_{t-1} + z - k)$$

where z = value at time t, normalized to a mean of 0 and a variance of 1, and k is a parameter that is often chosen to be equal to 0.5, or one half the standard deviation of the normalized the values. Therefore, only values more than 0.5 standard deviations above the expected value are accumulated in the CUSUM. An alert is signaled if $S_t > h$, where h is a threshold value chosen to balance sensitivity, specificity and timeliness. After an alert, the CUSUM is reset to zero and restarted.

A potential disadvantage of the CUSUM approach is that it assumes that the data follow a normal distribution and that observations are not serially correlated. Like

EWMA, CUSUM assumes that there are no systematic changes in the mean daily count over time. Rogerson and Yamada, however, describe an extension of CUSUM that assumes the data follow a Poisson distribution, and allows for seasonal effects [46].

Both CUSUM and EWMA were designed to detect small changes in average daily counts. Frisen demonstrated that EWMA yields the minimal expected delay in detection for a fixed false alarm probability, and CUSUM yields the minimal expected delay in detection for the "worst" history of observations before the outbreak occurred [47]. It is not clear which method is optimal for syndromic surveillance, and ESSENCE offers users the option of a CUSUM-based algorithm in addition to EWMA.

Scan statistics have been used by epidemiologists to detect disease clusters retrospectively for several decades [40]. Kulldorff [48] extended the method for prospective surveillance, and developed public domain software for this purpose called SatScan (available at www.satscan.org). SatScan can be used to conduct surveillance for outbreaks over time in a specific geographic region, but it can also be used to identify clusters of disease in space across geographic regions.

SatScan counts the number of events (e.g. outpatient visits, laboratory tests ordered) that took place within time interval d of the current time t, and compares the count to its expected value under a Poisson distribution. The scan statistic is defined as the largest likelihood ratio across all sets of distances d for which the count is greater than expected. The p-value for the scan statistic is obtained by Monte Carlo simulation, and an alert is sounded at time t if the p-value falls below a specified threshold. SatScan has been incorporated into many syndromic surveillance systems, including ESSENCE [8], the New York City DHMH [49] and the National Bioterrorism Syndromic Surveillance

Demonstration Program in Boston [50], mostly for spatial or spatio-temporal surveillance. Spatial surveillance is beyond the scope of this dissertation; we will focus on detecting temporal clusters within geographic locations defined by MTFs or groups of neighboring MTFs.

Other surveillance algorithms have been proposed, including hidden Markov models [51], wavelets [36], and Bayes belief nets [8]. So far, no single approach has dominated the others with respect to its ability to detect outbreaks, and research is ongoing. One study, for example, compared scan statistics with time series regression and spatial regression, and found that while the scan statistic performed best, a "smorgasbord" of methods was better than any individual method [52].

DoD-ESSENCE uses a combination of the methods described above. Linear regression models are fit to data from the previous month to remove time trends and weekend/holiday effects. If counts are small (typically, median < 5 per day), such as for a small MTF or a rare syndrome, regression models are likely to demonstrate lack of fit to the data, and the EWMA algorithm is run instead.

Triggering an alert

As described earlier, syndromic surveillance systems compare observed and expected values, and trigger an alert if observed values exceed expected values by at least a specified amount. The simplest approach to setting the threshold is based on *p*-values. An alert is given if the *p*-value for the difference between observed and expected values is less than 0.05, or 0.01. This corresponds roughly with the observed value being more than two or three standard deviations, respectively, above the expected value.

However, using a *p*-value of 0.05 or 0.01 will yield a false alert every 20 or 100 days on average. This concern is exacerbated by the problem of multiple comparisons. ESSENCE, for example, monitors seven syndromes in each of more than 300 MTFs every day. Even if the threshold for each syndrome and MTF is $p < 0.01$, DoD-ESSENCE can expect to see several false alerts every day. This high false alert rate places an undue burden on those who investigate alerts. In practice, public health personnel may not initiate an investigation unless an alert is sounded two days in a row for the same syndrome and MTF. This reduces the number of alerts that need to be investigated, but also reduces the timeliness of the investigation. Programmers can reduce the number of false alerts by incorporating multiple comparisons adjustments, such as the Bonferroni correction, into the algorithm. Again, this reduces the sensitivity and timeliness of the system.

A different approach is to set no explicit threshold for alerting. Some systems simply compile a daily list of counts ranked by their *p*-values, and note how many days each count has been higher than expected. Public health officials can scan the list and use their judgment to determine which counts to investigate. Advantages of this system are that it incorporates human judgment and it is acceptable to public health officials who use it, since they retain some control over which alerts to investigate.

Finally, an explicitly multivariate approach can be used to yield a combined alert. Possible multivariate approaches to syndromic surveillance are discussed below.

Multivariate extensions

A characteristic of the algorithms described so far is that they are used to monitor a single data stream. When more than one data stream is monitored, such as outpatient

visits and laboratory test orders in this study, the false alert rate will increase. Also, a slight increase in each of several data streams might not trigger an alert in any single data stream, but if the increase is consistent across several data streams, a multivariate method may be able to detect it. Several approaches have been considered, including parallel univariate surveillance, multivariate quality control methods, multivariate regression, and Bayes belief nets. A feature of all of these methods is that they produce a single *p*-value for the entire set of data streams, rather than an individual *p*-value for each data stream.

Parallel univariate surveillance involves using a surveillance algorithm to monitor each data stream separately, and combining the results to decide when an alert should be given. Combinations that have been considered are the maximum *p*-value, the product of *p*-values or the mean of *p*-values. Using the maximum *p*-value results in too many false alerts [8]. Fisher [53] proposed the product of *p*-values, which follows an approximate chi square distribution. Edgington [54] proposed calculating the mean of *p*-values, which follows an approximate normal distribution, and claimed that the mean of *p*-values is more powerful overall than the product of *p*-values. Burkom et al. found that both methods performed well in an outbreak detection simulation [55]. Fisher's method identified many alerts that were present in a single data stream, while Edgington's method consistently identified combined signals.

Multivariate control charts include Hotelling's T^2, multivariate CUSUM and multivariate EWMA (MEWMA). If the data streams follow a multivariate normal distribution, then a T^2 control chart may be appropriate [56]. T^2 is calculated using the following formula:

$$T^2 = n(y - \hat{y})'S^{-1}(y - \hat{y})$$

where y is the vector of observed counts, ŷ is the vector of expected counts, and S is the estimated covariance matrix of the two data streams, calculated from historical data.

Multivariate CUSUMs may be calculated in several different ways. The simplest is to use the T^2 statistic as the data for calculating the CUSUM; a direct multivariate generalization of the univariate CUSUM was proposed by Crosier [57]. MEWMA, described by Lowry et al. [58] uses the formula:

$$\hat{Y}_{t+1} = RY_t + (\mathrm{I}- R)\ \hat{Y}_t$$

where $\hat{Y}_t$ is the vector of counts at time t, R is a diagonal weight matrix, and I is the identity matrix.

Multivariate CUSUM and MEWMA have been shown to detect changes in the average value of the data stream more quickly than T^2. However, all three of these methods were found by Burkom to be too sensitive when used for syndromic surveillance [55]. These methods were likely to signal alerts after changes in the covariances among data streams, even if no change in the average daily counts occurred.

Another possible approach is multivariate regression. Methods for estimating multivariate time series and multivariate Poisson regression are well described in statistical texts [59, 60]. The generalized linear mixed model approach proposed by Kleinman et al. [42] to borrow strength across similar geographic regions could be adapted to borrow strength across related data streams.

ESSENCE developers have also explored the use of Bayes belief nets [8]. This approach estimates the joint probability distribution of all available data and estimates the probability of an outbreak from this distribution. The ESSENCE team applied Bayes

belief nets to test data, compared it with multivariate and parallel univariate control charts, and found the Bayes belief net to be versatile and robust [61]. Research on this method is ongoing. At present, we propose to use parallel univariate surveillance methods, but will monitor Burkom's ongoing research and consider any approach identified as promising.

Outbreak investigation

The final step in syndromic surveillance is investigating alerts to determine whether a disease outbreak is in fact occurring. Investigation may begin with a review of the data that triggered the alert, and may extend to calling hospitals and providers for information, or a full review of all identified cases. Some alerts may be resolved easily, such as a sudden increase in outpatient visits for Japanese encephalitis at a particular MTF that turned out to be a systematic miscoding of vaccinations for the disease [21]. Others require more extensive follow-up, such as outbreaks of gastrointestinal illness in which laboratory testing and food recall are initiated. The New York City DOHMH has found that syndromic surveillance is useful for citywide increases in illness, such as the annual influenza epidemic or large outbreaks of norovirus, but that small localized outbreaks are often missed [37]. DoD-ESSENCE detects gastrointestinal and respiratory outbreaks with some frequency, typically in larger MTFs that service recruit populations.

Evaluating syndromic surveillance systems

Syndromic surveillance systems are relatively new and their utility for detecting different sorts of disease outbreaks is unproven. If resources are to be devoted to syndromic surveillance systems, it is important to establish that they can achieve their stated goals. Also, if changes are to be made to existing systems, such as the change

proposed in this study, it is important to establish that the change improves the performance of the system. Since the stated goal of syndromic surveillance is early outbreak detection, systems should be evaluated with respect to ability to detect existing outbreaks (sensitivity) and to do so earlier than other methods (timeliness). Because it is always possible to improve sensitivity and timeliness by increasing the false alert rate (reducing specificity), and frequent false alerts reduce the utility of syndromic surveillance, specificity should be evaluated as well.

The CDC has established a framework for evaluating syndromic surveillance that addresses these aspects of system performance [7]. Evaluating sensitivity, specificity and timeliness requires data on well-defined outbreaks. For naturally occurring outbreaks, historical data may be used. Some outbreaks of interest for surveillance, such as those caused by bioterrorism, are not available in historical data and must be simulated. Outbreaks may be simulated by superimposing a simulated outbreak on authentic background data, or by simulating both outbreaks and background data. A final approach to evaluation is to superimpose authentic outbreaks on simulated background data. These approaches are outlined in Mandl et al. [62].

We use historical data including real outbreaks for this evaluation . An advantage of this approach is that no assumptions must be made about the shape of the epidemic curve or the distribution of the background data. One potential disadvantage is that outbreaks due to bioterrorism may not resemble naturally occurring outbreaks, so the ability of a surveillance system to detect naturally occurring outbreaks may not extend to its ability to detect bioterrorist attacks. However, early symptoms of some pathogens

likely to be used by bioterrorists may match symptoms of respiratory and gastrointestinal outbreaks [63].

In the evaluation framework, once outbreaks are defined, the syndromic surveillance algorithm is run on data that contain these outbreaks. For each outbreak, it is determined whether an alert was signaled, which days of the outbreak were identified, and on which day the alert was first given. Sensitivity and specificity may be calculated across all outbreaks, or across all outbreak days, using the standard formulas. Timeliness is often defined as the mean (or median) number of days between the first day of the defined outbreak and the first alert.

Timeliness depends in part on how quickly the following events take place: an exposed patient seeks medical care; the provider orders laboratory tests; the laboratory tests are entered into the electronic database, transmitted to the central server, and analyzed; and the results are used to inform public health investigations. A tabulation of laboratory test orders shows that for 90 percent of completed microbiology laboratory tests, specimens were collected on the same day that the test was ordered. Because laboratory tests in the DoD system must be entered into an electronic database before the specimen is tested, data could be transmitted and analyzed in near real time. Whether or not laboratory test orders provide timely indication of disease outbreaks may depend more on how often and how early in the course of disease the laboratory tests are ordered. If laboratory tests are only ordered in later stages of disease, then surveillance using laboratory test order data may still be useful for confirming and investigating outbreaks, but is unlikely on its own to lead to early detection. Comparing the timeliness of

surveillance using two data sources, laboratory test orders and outpatient visits, can shed light on this question.

An aspect of validity that is not directly addressed in the CDC's framework is the validity of syndrome definitions. In other words, are we monitoring the right laboratory tests to identify patients with signs and symptoms of particular syndromes? The syndrome definitions proposed by the CDC's working group (Appendix 1) have face validity in that experts think that the tests in each syndrome are likely to be ordered when the patient presents with signs and symptoms associated with that syndrome. To establish criterion validity, we compare laboratory test orders against outpatient visit volume for the same syndrome. Discriminant validity will be based on low correlations with other syndromes, at least relative to correlation with the assigned syndrome.

Syndromic surveillance systems must also be evaluated in practice: Are they acceptable to public health workers who use them? Are they flexible, portable, and stable? Are they cost effective? We believe that adding laboratory test order data to DoD-ESSENCE would not greatly affect system operating characteristics. ESSENCE II, a version of ESSENCE that combines military and civilian data sources for surveillance in the Washington, DC area, has been evaluated with respect to these criteria [12]. This study uses retrospective analysis to assess validity, and leaves prospective studies of system experience for future research.

Summary

This chapter has described the definition and goals of syndromic surveillance, data sources, syndrome definitions, alerting algorithms, and evaluation methods. This study uses a new data source, develops and validates syndrome definitions for this data

source, applies existing surveillance algorithms using this data set, and evaluates the results. The next chapter will discuss the methodology in detail.

CHAPTER III: Materials and Methods

As stated above, the purpose of this study is to evaluate whether data on microbiology laboratory tests ordered for patients by providers during outpatient visits to military treatment facilities (MTFs) can improve the performance of ESSENCE in detecting disease outbreaks. Improved performance is measured by sensitivity, specificity and timeliness of outbreak detection. This section details the materials and methods used in the study, including data sources, statistical analysis, and evaluation criteria.

Description of data

Data for this project consist of administrative records obtained from two sources: laboratory test records from the Executive Information and Decision Support Program Office (EI/DS) of TRICARE, and outpatient visit data from DoD-ESSENCE. EI/DS has provided data on microbiology laboratory test orders, excluding HIV tests, from outpatient MTFs worldwide. Data are available from November 2002 to November 2004. WRAIR biostatisticians provided access to DoD-ESSENCE automated ambulatory military health system visit data for the same time period.

The target population for this study is all active duty military, military retirees, and family members who are eligible to receive care in military treatment facilities. Subjects represent all age groups, both male and female. No power analysis was performed, since we obtained all records rather than a sample of records. The complete data set contains records for 3.4 million microbiology laboratory tests on 1.2 million patients.

We characterize the data with respect to person (age, sex, branch of service, relationship to military sponsor), place (military treatment facility and clinic type), and time (weekly and seasonal patterns, and time lags between test order, specimen collection, and test result).

Figure 3.1 illustrates the process by which a laboratory test is archived in the database. Because test information can be "lost" at any point in the process, the archive of data used in this study does not include all test orders. While it is impossible to ascertain exactly how many tests are ordered but never archived, discussions with laboratory personnel suggest the number of such tests is low relative to the total volume of tests. Uncommon laboratory tests may be sent to non-DoD laboratories, but if they were ordered within the DoD system, they should be entered into the database when the results are returned. Laboratory tests ordered for DoD beneficiaries by civilian providers will not be archived in the database unless the tests are sent to a DoD laboratory. However, because TRICARE provides better coverage for tests performed in a DoD laboratory, it is likely that many tests ordered by civilian providers are sent to DoD labs. This study will treat the archived laboratory tests as if they represent all tests ordered, and analyze them based on the date of order rather than the date on which they were archived.

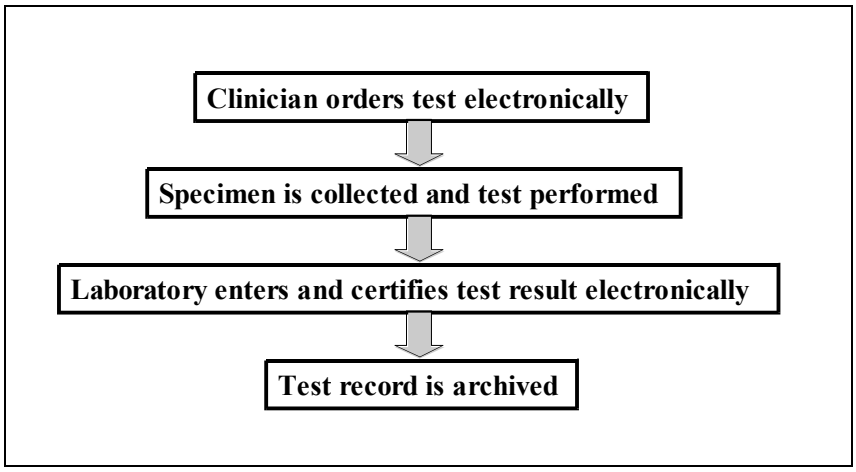


Figure 3.1: DoD Laboratory Ordering Process

Coding laboratory test descriptions

The DoD does not currently use a standard reporting system for laboratory test orders. Laboratory ordering and reporting systems are developed by region, and within a region the reporting system may require the provider to select the appropriate laboratory test from a list, or may allow free text. As a result, a single type of test may be reported in many different ways, including multiple spellings and abbreviations. For example, in a preliminary sample of the DoD data, rapid strep tests were indicated in at least six different ways: 'RAP STRE', 'RAP STREP', 'RAPID ST', 'RAPID STREP', 'RAPID STREP A', and 'RAPSTP&C'.

We will develop a standard nomenclature to account for different spellings and abbreviations. First, test names will be grouped using a list of common synonyms. Second, test names that do not appear on the list of synonyms will be assigned by hand to an existing category, or a new category will be created. Third, test orders for which the test name contains insufficient information will be assigned to a category based on

specimen source where possible. For example, a "miscellaneous culture" for which the specimen source is "stool" will be considered a "stool culture." Finally, multiple tests for the same illness will be combined into a single category.

Subject identification and human use

Access to the data extracted for use in this project was provided through a password protected network drive shared within the security of the WRAIR firewall. Data were provided to WRAIR after removal of all identifying information by EI/DS programmers. Records for a subject may be linked using an encrypted pseudo-identifier unique to the subject; however, the research team does not, and will not, have the password to reverse the encryption, thus cannot obtain any identifying information on individual subjects. The data analysis was conducted at WRAIR, USUHS or from the PI's personal computer. Data are reported only in the aggregate.

In addition to information about specific laboratory tests and diagnostic codes, the initial data files contain the following demographic information for each record: age (in years; date of birth will not be on the file), sex, branch of service, relationship to military sponsor, MTF, and 5-digit ZIP code (the 5-digit ZIP code is not used in this analysis).

Data analysis

This study relies primarily on descriptive, correlational analysis, along with time series and quality control methods. SAS® is used for data manipulation, graphical comparisons and statistical analyses.

Validating syndrome definitions

The *first specific aim* is to identify laboratory tests that may be associated with disease outbreaks, and with other measures of disease prevalence. Our primary measure

of disease prevalence is DoD-ESSENCE syndrome counts based on outpatient ICD-9 codes. The data used to construct these syndrome counts are based on physician diagnoses rather than patient chief complaint, and have been shown to correspond well with physician assessments of disease from chart reviews [13]. We examine the association between the CDC-defined laboratory test syndromes and DoD-ESSENCE's ICD-9 code based syndromes, and will also explore associations between individual laboratory tests and ICD-9 code based syndromes. We will examine the association between laboratory test orders and outpatient visit diagnoses from three different perspectives.

At the level of the individual outpatient visit, we will use data on type of laboratory test ordered (from laboratory test data) and ICD-9 diagnostic codes recorded during the outpatient visit in which the test was ordered (from ESSENCE outpatient visit records). Records from laboratory test data will be linked with outpatient visits based on pseudo identifiers and date of visit/test order. We will identify the disease syndromes associated with each outpatient visit using the ICD-9 diagnostic codes for that visit and DoD-ESSENCE syndrome definitions (Appendix 3). Contingency tables will be constructed for each syndrome and laboratory test of interest, with cell counts corresponding to the number of outpatient visits in each category:

	Test ordered?	
Syndrome present?	Yes	No
Yes	a	b
No	c	d

For each syndrome, laboratory tests will be ranked according to strength of association with that syndrome, where strength of association is measured by the ratio of

observed number of visits with the syndrome in which the test was ordered, compared with the expected number if laboratory tests ordered were independent of outpatient visit diagnosis. (The expected count is calculated as [a+b]*[a+c]/[a+b+c+d].) Tests that are strongly associated with each syndrome will be considered for surveillance of that syndrome.

The second approach will examine daily volume of laboratory test orders and outpatient visits over time. We will construct daily counts for each laboratory test over the period of the study, and will construct daily counts of outpatient visits for each syndrome over the same time period. Spearman's rank correlation will be used to measure the strength of association over time between each laboratory test and each ICD-9 code based syndrome. We will consider overall correlation and "residual" correlation, after removing secular trends, seasonal and/or weekly patterns from the data [19]. This will allow us to distinguish between correlation due to similar cyclical patterns of disease and health care seeking behavior, and correlations due to unexpected changes in disease patterns. For each syndrome, laboratory tests will be ranked according to strength of association with that syndrome, and tests that are most strongly associated with each syndrome will be considered for surveillance.

To determine which laboratory tests (or combinations of laboratory tests) are most strongly associated with disease outbreaks, we will examine daily counts of laboratory test orders during known outbreaks. The strength of association with an outbreak will be measured by the ratio of the average daily count of laboratory tests ordered during the outbreak to the average daily count of laboratory tests ordered during a comparable non-outbreak period, such as a period of the same length immediately preceding the outbreak.

Outbreaks identified by ESSENCE epidemiologists during the period from November 2002 to November 2004, in MTFs which provided HL7 records during that period, will be used. Specific outbreaks are listed in chapters 4 and 5 below.

Evaluating outbreak detection performance

The second specific aim is to develop and compare several strategies for using laboratory test orders for syndromic surveillance, alone and in combination with outpatient visit data. One or more laboratory tests or syndromes identified under the first specific aim will be used for this analysis. Below we outline and discuss the components of the surveillance system to be used.

Surveillance algorithm: Several off-the-shelf algorithms are available for syndromic surveillance. We propose to use the DoD-ESSENCE algorithm in order to make the results of the study most relevant for DoD-ESSENCE planners in the future. We also consider the CUSUM algorithms implemented in the CDC's EARS, a temporal scan statistic, and a simple EWMA algorithm, since these algorithms are freely available to the public.

The DoD-ESSENCE algorithm is described above, and is discussed in detail elsewhere [8, 21]. The two main components of this algorithm are regression and EWMA. In the regression model, day of the week, holiday, and time trend will be considered as independent variables, and the dependent variable will be daily counts. We will also use the EWMA algorithm currently in use by the DoD-ESSENCE system, including the parameters that are specified by this algorithm. Finally, we will examine whether regression models tend to fit the data well, or if running the EWMA algorithm

on the raw data is generally sufficient. Performance will be evaluated as described below.

Threshold for alerting: In general, as the threshold for alerting is raised, false alarms will be less frequent (increased specificity) but smaller outbreaks are more likely to be missed (decreased sensitivity) and slow-building outbreaks will be caught later in their development (decreased timeliness). For evaluation purposes it is not necessary to specify a single threshold for alerting; instead, the tradeoffs among sensitivity, specificity and timeliness will be explored in detail.

Combining data sources: It is possible that laboratory test order data are entered and transmitted more quickly than outpatient data under the current electronic system. In a version of CHCS that is still under development, however, laboratory test data will be entered and transmitted along with outpatient and pharmacy data in a single record. For this reason, we do not expect future laboratory test order data to provide an earlier signal than these data sources when an outbreak occurs. However, laboratory test order data may strengthen the ratio of signal to noise to improve the probability of detecting outbreaks. To take advantage of this possibility, we will look at laboratory test order data in combination with outpatient visit data. Parallel univariate surveillance algorithms will be run separately on outpatient visits and laboratory test data, and *p*-values will be combined to obtain an overall *p*-value comparing observed events to expected events. We will consider the methods of Edgington [54] and Fisher [53], described in the background section.

Evaluate the strategy with respect to outbreak detection (sensitivity, specificity and timeliness): The surveillance algorithm(s) will be evaluated on data containing known

outbreaks. Two sources of outbreaks have been considered: simulated outbreaks, in which hypothetical outbreaks are superimposed onto existing data; and naturally occurring outbreaks, which use laboratory test order data for dates, MTFs and syndromes corresponding to a set of known outbreaks. We propose to use data on naturally occurring outbreaks because these data reflect actual patterns of illness, not hypothetical ones. Furthermore, simulating realistic outbreaks in laboratory test data requires a detailed model of the complex relationships among exposure, illness, healthcare-seeking behavior, and laboratory test ordering patterns. The proportion of outpatient visits in which lab tests are ordered, the specific symptoms for which each test is likely to be ordered, and whether ordering behavior changes during an outbreak, are all unknown, so simulating the effects of an outbreak on laboratory test orders would be difficult.

Unfortunately, all confirmed outbreaks identified during the study period correspond to respiratory and gastrointestinal syndromes. A weakness of this study is that our ability to evaluate sensitivity, specificity and timeliness is limited to these two syndromes. We will use case studies of non-confirmed outbreaks to describe patterns of laboratory test orders for these syndromes. Even though confirmed outbreaks have not been identified for all syndromes, this research will provide an important first look at the usefulness of the laboratory test data.

We will evaluate the performance of the algorithms with respect to timeliness, sensitivity and specificity. The surveillance algorithm will be run on the data with known outbreaks and we will monitor whether (and how quickly) the algorithm detects outbreaks, and how often the surveillance algorithm triggers a false alert. Modified receiver operating characteristic (ROC) curves, which plot sensitivity against background

alert rate, will be used to illustrate the tradeoff between sensitivity and specificity. The background alert rate is defined as the average number of days between alerts that do not correspond to a verified outbreak (e.g., one alert every six weeks). We assume that the longer the period between background alerts, the greater the specificity. We cannot measure specificity directly because some alerts may correspond to true outbreaks that were not verified by public health personnel. We will also report sensitivity and timeliness for specific background alert rates ranging from one alert every two weeks to one alert every eight weeks.

CHAPTER IV: Development and evaluation of laboratory test nomenclature and syndrome definitions

Introduction

The first specific aim of this study is to identify laboratory tests that may be associated with disease outbreaks, and with other measures of disease prevalence. We will identify laboratory tests that meet the criteria outlined below:

- The laboratory test is more likely to be ordered during an outpatient visit in which the patient is diagnosed with a disease syndrome under surveillance by ESSENCE, than during an outpatient visit in which no such syndrome is diagnosed.
- Daily counts of the laboratory test are positively correlated over time with daily counts of outpatient visits for one or more of the disease syndromes under surveillance by ESSENCE.
- Daily counts of the laboratory test are higher during disease outbreaks than during non-outbreak periods.

The purpose of this chapter is to evaluate laboratory tests with respect to these criteria and propose individual laboratory tests, or syndrome groupings comprised of several related laboratory tests, for surveillance.

Description of data

Data consist of all outpatient microbiology lab tests with a certified result that were entered into the CHCS I system between November 2, 2002 and October 31, 2004. Data include tests for active duty military personnel, their dependents, and retirees from

all branches of service at MTFs worldwide. Characteristics of laboratory tests and the patients for whom they were ordered are described in Table 4.1.

Table 4.1: Characteristics of laboratory tests and patients used in the analysis

		% of tests	% of patients
Sex	Female	67.8	61.1
	Male	32.2	38.9
Age (years)	0-4	8.7	9.0
	5-17	15.7	17.7
	18-64	70.9	69.2
	65+	4.7	4.1
Relationship to military sponsor	Child	28.3	30.2
	Sponsor	34.9	37.0
	Spouse	36.6	32.5
	Other	0.2	0.3
Branch of service	Army	33.2	33.5
	Air Force	24.6	25.2
	Marine Corps	12.8	13.0
	Navy	27.0	25.8
	Other	2.4	2.5
Type of clinic	Emergency	17.2	
	Primary care	62.3	
	Other outpatient	20.5	
N		1,825,194	1,003,338

The CHCS II system stores laboratory data in a hierarchical file with multiple records for each lab test. Basic information, including test ordered, specimen source, MTF, and demographics of the patient are repeated in each record for a single test. Multiple records for the same test differ primarily with respect to the test result; for example, growth of a culture may be observed on several different days, with one record for each observation; or sensitivity to several antibiotics may be tested, with one record for each antibiotic. Since the test results will not be used for syndromic surveillance, the

first step in processing the data was to collapse the file so that it contains a single record for each laboratory test.

Next, a subset was selected on the basis of date and MTF. This analysis included tests ordered from November 2002 through October 2004. Of 325 land-based MTFs that recorded at least one laboratory test in the CHCS I database, 112 either did not start reporting until after June 2004, or had significant gaps in reporting during the November 2002-October 2004 time frame. The analysis sample is restricted to the remaining 214 land-based MTFs with complete data (Appendix 2). Completeness was determined through examination of time series plots of daily laboratory test order counts for each MTF, and tabulation of first and last order dates for each MTF. One MTF with complete data, the USS Eisenhower, will not be included because it is the only ship that submitted laboratory records.

Data on outpatient visits to MTFs were obtained for comparison purposes. Visit date, MTF, patient age and sex, ICD-9 diagnostic codes, and encrypted identifiers for the patient and provider were obtained from CHCS standard outpatient data records (SADR). All outpatient visits to the 214 included MTFs during the study period were selected. Each outpatient visit was evaluated for assignment to one or more syndrome categories based on recorded ICD-9 codes. DoD-ESSENCE syndrome definitions from January 2004 were used for syndrome assignment (Appendix 3).

Test order standardization

Different MTFs use different abbreviations to describe the same test. For example, sputum cultures were recorded as “SP CULTURE”, “SPU CULT”, “SPUT C&S/SMEAR”, or simply, “SPUTUM”. A total of 870 distinct test order names appear

in the laboratory test data archive from November 2002 through October 2004. These were categorized into 71 standard test names, using the following process:

- Dr. Julie Pavlin obtained from Major Martin Tenney a standardized list of DoD microbiology lab tests (Appendix 4). Major Tenney is part of an initiative to standardize lab test orders in CHCS. He also provided a list of common synonyms for the lab tests on the standardized list. Overall, 73% of the lab tests descriptions in the laboratory data match his standardized list or one of the synonyms he provided.
- Major Tenney's list included separate categories when different tests could be ordered for the same illness. For example, in his list, ANTHRAX PHAGE, ANTHRAX CULTURE, ANTHRAX DFA, AND B ANTHRACIS ID are all listed as separate tests. Drs. Julie Pavlin, Shilpa Hakre, and J.D. Malone reviewed the list and recommended which categories could be combined for the purpose of surveillance.
- Major Tenney's list does not include large categories of tests that are represented in the data set. New categories were created for acinetobacter, acid-fast bacilli, fecal reducing substances, fecal occult blood, fecal white blood cells, Group A streptococcus, Group B streptococcus, herpes, influenza, blood parasites and leishmaniasis. A handful of tests on his list, such as tests for *Calymmatobacterium* or *Klebsiella granulomatis* and *Coccidioides*, do not occur in this data set so were discarded.

- Test order names that do not match a name or synonym on Major Tenney's list were reviewed by Dr. Hakre and Dr. Malone and assigned to one of his categories, or to a new category as necessary.
- Some test order names contain insufficient information to assign to a category, e.g. MISC CULTURE or BODY FLD CULTURE. Records corresponding to these test order names were examined to determine the source of the specimen. If the specimen source was urine, blood, cerebrospinal fluid, feces, pharynx, sputum, nose, or wound, the test was assigned to the category corresponding to a standard culture of the specimen.

Appendix 5 summarizes the mapping of the 870 observed test names to 71 standard test names.

Criterion #1: Laboratory test/syndrome co-occurrence

Laboratory test data and outpatient visit data were merged in order to determine which lab tests were most commonly associated with which diagnoses. A laboratory test record was matched to an outpatient visit record by encrypted patient identifier (military sponsor's encrypted SSN and patient's family member prefix) and date (within two days). In order to minimize duplicate matches, the following steps were taken:

- Records for pending laboratory tests were excluded. CHCS contains separate records for pending and final test results, with different codes. (26% of laboratory test records were excluded under this criterion).
- If a patient saw two or more different providers for the same syndrome for the same day, only the record corresponding to the first visit was retained. (9% of outpatient records were excluded under this criterion.)

- If a lab test was matched to two or more outpatient visits on different days, the visit date closest to the date on which the lab test was ordered was retained.
- If a lab test was matched to two or more outpatient visits on the same day, one of the outpatient visits was selected at random for inclusion.

Outpatient visits and tests that occurred from May 2003 through April 2004 were included in this analysis. (Memory limitations on the secure server precluded matching the entire two years of data.) A total of 18,579,731 records were examined. Of these, 0.7 percent (122,685 records) correspond to a laboratory test record that could not be matched to an outpatient visit. Possible explanations are that the laboratory test was ordered more than two days after the visit, it was not ordered in conjunction with a visit, or the data were entered incorrectly. Because these records are such a small proportion of the data, we did not investigate potential explanations further. Eighty-six percent (15,945,889 records) correspond to an outpatient visit that was neither assigned to a syndrome nor matched to a corresponding laboratory test. These include routine visits and visits with no diagnosis of infectious disease. Ten percent (1,870,977) correspond to a visit that was assigned to a syndrome on the basis of ICD9 codes but for which no laboratory tests were ordered. The remaining 3.4 percent (640,181 records) correspond to an outpatient visit with a matched laboratory test.

In order to identify laboratory tests that were most likely to be ordered during outpatient visits for each syndrome, we crosstabulated the merged laboratory test and outpatient visit file by laboratory test name and syndrome. We calculated expected counts in each cell in the table under the assumption that laboratory test orders were not associated with syndrome diagnosis. If the ratio of observed to expected counts in a cell

was 2.0 or greater, the corresponding laboratory test and syndrome were determined to be associated. Table 4.2 lists laboratory tests associated with each syndrome under this criterion.

The most notable pattern is that aerobic blood cultures and unspecified blood cultures are associated with all syndromes except botulism-like illness. Ordering patterns across syndromes are similar for these two tests, so they may be used interchangeably by different MTFs. Although the strongest association is for the fever and shock/coma syndromes, the two tests combined are five times more likely to be ordered when any infectious disease syndrome is diagnosed than when no such syndrome is diagnosed. Aerobic blood cultures may be an indicator, therefore, for the presence of any infectious disease but may not differentiate well among disease syndromes.

Table 4.2: Observed vs. expected number of test orders

Syndrome	*std_test_ord*	*Obs/exp ratio*
Bot_like	BF CULT	5.49
	CSF CULTURE	4.77
	EAR CULT	3.75
	SPUTUM CULT	3.40
Fever	AER BLD CULT	28.53
	ANAER BLD CULT	16.17
	BLD CULT	20.24
	BLD PARA	21.66
	BORDETELLA CULT	4.05
	C DIFFICILE	6.05
	CSF CULTURE	19.90
	E COLI O157:H7	10.79
	EYE CULT	2.46
	FECAL WBC	2.03
	FUNGUS, CSF	8.34
	GRAM STAIN	7.59
	GROUP A STREP	8.50
	INFLUENZA	25.27
	OTHER	2.33
	ROTAVIRUS	7.05
	RSV	10.78
	SSC	2.32
	STOOL CULT	2.35
	THR CULT	6.55
	UA CULT	3.45
	VIRAL CULT	5.92
	YERSINIA CULT	2.62
GI	AER BLD CULT	3.70
	ANAER BLD CULT	2.63
	BLD CULT	3.05
	BLD PARA	3.98
	C DIFFICILE	28.51
	CMV	5.15
	CSF CULTURE	2.01
	E COLI O157:H7	16.96
	FECAL RS	16.02
	FECAL WBC	43.10
	FOB	2.02
	GIARDIA/CRYPTO	13.33
	H PYLORI CULT	12.55
	O & P	17.67
	OTHER	2.91
	OTHER GI	28.79
	ROTAVIRUS	44.35
	SSC	40.14
	STOOL CULT	38.49
	VIBRIO	46.42
	YERSINIA CULT	14.41
Hemr_ill	AER BLD CULT	8.02
	ANAER BLD CULT	4.91
	ANAER CULT	2.42
	H PYLORI CULT	3.04
Neuro	AER BLD CULT	2.60
	ANAER BLD CULT	14.34
	BF CULT	40.59
	BLD CULT	4.73
	CSF CULTURE	471.93
	FUNGUS, CSF	600.63
	FUNGUS, OTHER	7.32
	GRAM STAIN	134.80
	HERPES	12.87
	OTHER	14.11
	VARICELLA	337.09
	VIRAL CULT	17.91
Rash	AER BLD CULT	5.60
	AEROBIC CULT	3.55
	ANAER CULT	4.56
	BLD CULT	3.63
	BLD PARA	5.10
	FUNGUS, OTHER	2.62
	GROUP A STREP	4.11
	HERPES	3.87
	MISC CULTURE	6.33
	THR CULT	3.46
	TISSUE CULT	6.15
	VARICELLA	36.23
	VIRAL CULT	28.88
	WND CULT	4.58
Resp	AER BLD CULT	3.54
	ANAER BLD CULT	2.56
	BLD CULT	3.46
	BORDETELLA CULT	8.03
	EAR CULT	5.38
	GROUP A STREP	7.35
	INFLUENZA	6.02
	RECTAL CULT	7.59
	RESP CULT	4.62
	RESP CULTURE	5.44
	RSV	7.31
	SPUTUM CULT	6.16
	THR CULT	7.28
	VIRAL CULT	2.74
Shk_Coma	AER BLD CULT	11.54
	AEROBIC CULT	2.44
	BF CULT	16.36
	BLD CULT	32.19
	CSF CULTURE	7.12
	GRAM STAIN	6.23
	O & P	3.08
	SPUTUM CULT	15.23
	STOOL CULT	3.57
	UA CULT	2.27
	WND CULT	2.10

We compared strong test/syndrome associations with those identified by a CDC expert panel [23], based on a consensus method (Appendix 1). Most associations identified by the CDC expert panel were also observed in the DoD data set. However, there were several exceptions:

- The CDC panel associated aerobic and anaerobic cultures (other than blood cultures) and MRSA tests with fever, but those associations were not observed in the DoD data. Definitions of the aerobic and anaerobic cultures may differ in the two data sets; in this case, the CDC laboratory data do not seem to differentiate between aerobic cultures of blood and of other body fluids. Three-hundred ninety MRSA tests were ordered in the DoD data set, and only three were associated with a syndrome diagnosis: one with fever, and two with respiratory.
- The CDC panel associated viral cultures with fever, GI, rash` and respiratory syndromes. This analysis identified associations with fever, neurological, rash, and respiratory syndromes but not GI syndrome.
- The CDC panel associated cultures of Brucella, Chlamydia, respiratory fungus, legionella, and mycoplasma with respiratory syndrome, but these associations were not observed in the DoD data. The total number of Brucella, Legionella and Mycoplasma cultures reported during the two years of the study is less than 10, so this should not be considered evidence against the existence of these associations. Chlamydia and respiratory fungus cultures, however, were ordered 172 and 156 times, respectively.

This analysis identified several laboratory test/syndrome associations that were not identified by the CDC expert panel:

- The CDC expert panel did not identify any associations between laboratory tests and the botulism-like illness syndrome. The DoD data included 7,943 diagnoses of botulism-like illness syndrome, of which only 55 (<1%) had an associated laboratory test order. However, within this small subgroup, botulism-like illness was associated with cultures of body fluid, cerebrospinal fluid, ear, and sputum.
- Several associations with the fever syndrome did not correspond to the CDC panel's recommendations, including bordetella, c. difficile, E. coli O157:H7, fecal WBC, fungus in CSF, group A strep, influenza, rotavirus, RSV, SSC, stool, throat, urine, CSF, eye, and Yersinia cultures.
- Gastrointestinal syndrome was associated with aerobic and anaerobic blood cultures, blood parasite tests, CMV, and CSF cultures.
- The CDC expert panel did not identify any associations between laboratory tests and the hemorrhagic illness syndrome. The DoD data included 11,494 diagnoses of hemorrhagic illness syndrome, of which 305 (2.7%) were associated with a laboratory test order. Standard blood cultures are associated with this syndrome, as is H. pylori culture. However, the H. pylori association is based on only two laboratory test orders.
- Most of the tests associated with neurological illness by the CDC expert panel do not appear in the DoD microbiology data. These include specific tests for West Nile Virus, Lyme disease, and several types of encephalitis, which may be recorded with chemistry lab tests. However, this analysis indicates that neurological syndrome diagnoses are associated with viral,

blood and body fluid cultures; Gram stains; and tests for fungus (other than CSF, genital or respiratory), herpes, and varicella.

- The microbiology data do not capture the tests for specific illnesses in the rash syndrome, except for herpes and varicella. However, associations are seen between the rash syndrome and several general tests that were not identified by the CDC expert panel. These include blood cultures, blood parasites, fungus (other than CSF, genital or respiratory), group A strep, and throat, tissue, viral, wound and miscellaneous cultures.
- Blood, rectal and ear cultures are the only associations with respiratory syndrome that were observed in the DoD data but not identified by the CDC expert panel.
- The CDC does not use the shock/coma syndrome defined for DoD-ESSENCE, so the expert panel did not consider associations with this syndrome. This analysis indicates that Gram stains, ova/parasite tests, and cultures of blood, body fluids, CSF, sputum, stool, urine and wounds are associated with this syndrome. Patients presenting with this syndrome may be very ill and providers may be inclined to order any and all general tests for these patients.

In summary, agreement between the CDC expert panel and the data is quite high. Exact agreement cannot be calculated since the two data sets do not include exactly the same list of tests. This analysis identified a set of tests that seems to be associated with infectious disease in general, and validated associations between specific tests and syndromes.

Criterion #2: Time series correlations

In order to identify laboratory tests that are correlated over time with particular syndromes, we chose to focus on data from six regions. Overall time series correlations for all MTFs combined were not particularly useful because there is so much variability across MTFs. We chose military hospitals from different regions and branches of service, along with their associated clinics, in order to explore how time series correlations might vary by region, service, and MTF size.

Fifty-six MTFs in six regions were selected for evaluation under criterion #2. Each region consists of one or more military hospitals, and nearby clinics that support the hospitals. These MTFs were selected from among the 214 land-based MTFs with complete data to represent different geographic locations and branches of service. Table 4.3 lists the hospitals and clinics in each selected region, along with the median daily number of lab tests ordered in each.

Table 4.3: Description of regions selected for time series analysis

Region	*Facility type*	*Facility name*	*Median daily laboratory test orders*
Ft. Benning	Hospitals	MARTIN ACH	114
	Clinics	RECEPTION STA. TMC-FT. BENNING	0
		TMC-1-FT. BENNING	1
		TMC-2-FT. BENNING	0
		TMC-5-FT. BENNING	2
		TMC-7-FT. BENNING	2
		WINDER FPC	14
Hawaii	Hospitals	TRIPLER AMC	94
	Clinics	15th MEDICAL GROUP	10
		BMC MCAS KANEOHE BAY	7
		NBHC MCB CAMP H.M. SMITH	0
		NBHC NAVCAMS EASTPAC	0
		NHC PEARL HARBOR	27
		SCHOFIELD BARRACKS AHC	27
		TMC-1-SCHOFIELD 25th	5
NCA	Hospitals	89th MEDICAL GROUP	61
		NNMC BETHESDA	79
		WALTER REED ARMY MEDICAL CENTER	59
	Clinics	11TH MEDICAL GROUP	10

Region	*Facility type*	*Facility name*	*Median daily laboratory test orders*
		ANDREW RADER AHC	11
		BMC WILLOW GROVE	1
		DEWITT ACH	52
		DILORENZO TRICARE HEALTH CLINICS	7
		FAMILY HEALTH CENTER FAIRFAX	24
		FAMILY HEALTH CENTER WOODBRIDGE	44
		KIMBROUGH AMBULATORY CARE CENTER	30
		KIRK AHC	10
		NBHC ANDREWS AFB	0
		NBHC DAHLGREN	0
		NBHC INDIAN HEAD	1
		NHC ANNAPOLIS	7
		NHC PATUXENT RIVER	11
		NHC QUANTICO	26
Pensacola	Hospitals	NH PENSACOLA	56
	Clinics	NBHC MILTON WHITING FIELD	3
		NBHC NAS PENSACOLA	3
		NBHC NATTC PENSACOLA	8
		NBHC NTTC PENSACOLA	2
San Diego	Hospitals	NH CAMP PENDLETON	46
		NMC SAN DIEGO	112
	Clinics	BMC CAMP DELMAR MCB	0
		BMC CORCEN MCB	0
		BMC EDSON RANGE ANNEX	3
		BMC MCAS MIRAMAR	13
		BMC MCB CAMP PENDLETON	0
		BMC SAN ONOFRE MCB	1
		NBHC CORONADO	0
		NBHC EL CENTRO	0
		NBHC MCRD SAN DIEGO	8
		NBHC NAS NORTH ISLAND	5
		NBHC NAVSTA SAN DIEGO	5
		NBHC NTC SAN DIEGO	12
		TRICARE OUTPATIENT-CHULA VISTA	19
		TRICARE OUTPATIENT-CLAIRMONT	17
		TRICARE OUTPATIENT-OCEANSIDE	4
Wright-Patterson	Hospitals	74th MEDICAL GROUP	79
All hospitals			67
All clinics			4
All MTFs			7

Daily time series were constructed for each laboratory test and outpatient visit syndrome by region. The time series covers the two-year period from 1 November 2002 through 31 October 2004. For each day of the study period, the number of outpatient

visits for each syndrome and the number of each of the 71 laboratory tests were counted for each region.

Clinics typically order a small number of laboratory tests every day. The median number of laboratory tests ordered, across selected clinics for two years, is only four per day. Time series correlations among series with such small counts are quite low, and may reflect the sparseness of the data more than any lack of association between outpatient visits and laboratory test orders. However, combining clinic data with data from nearby hospitals may be a good way to evaluate regional ordering patterns. All correlations for this specific aim will be performed at the regional level.

Both hospitals and clinics tend to order more tests on weekdays than on weekends. This pattern has been observed in multiple syndromic surveillance data sources (e.g. Lazarus, 2001[ref]) and is illustrated in Figure 4.1. In the selected DoD hospitals, laboratory tests are three times more likely to be ordered on weekdays than on weekends, and in clinics the weekday/weekend ratio is even higher. For common laboratory cultures the weekday/weekend ratio ranges from 1:1 to one for blood tests in hospitals to more than 4:1 for throat, wound, and stool cultures in clinics.

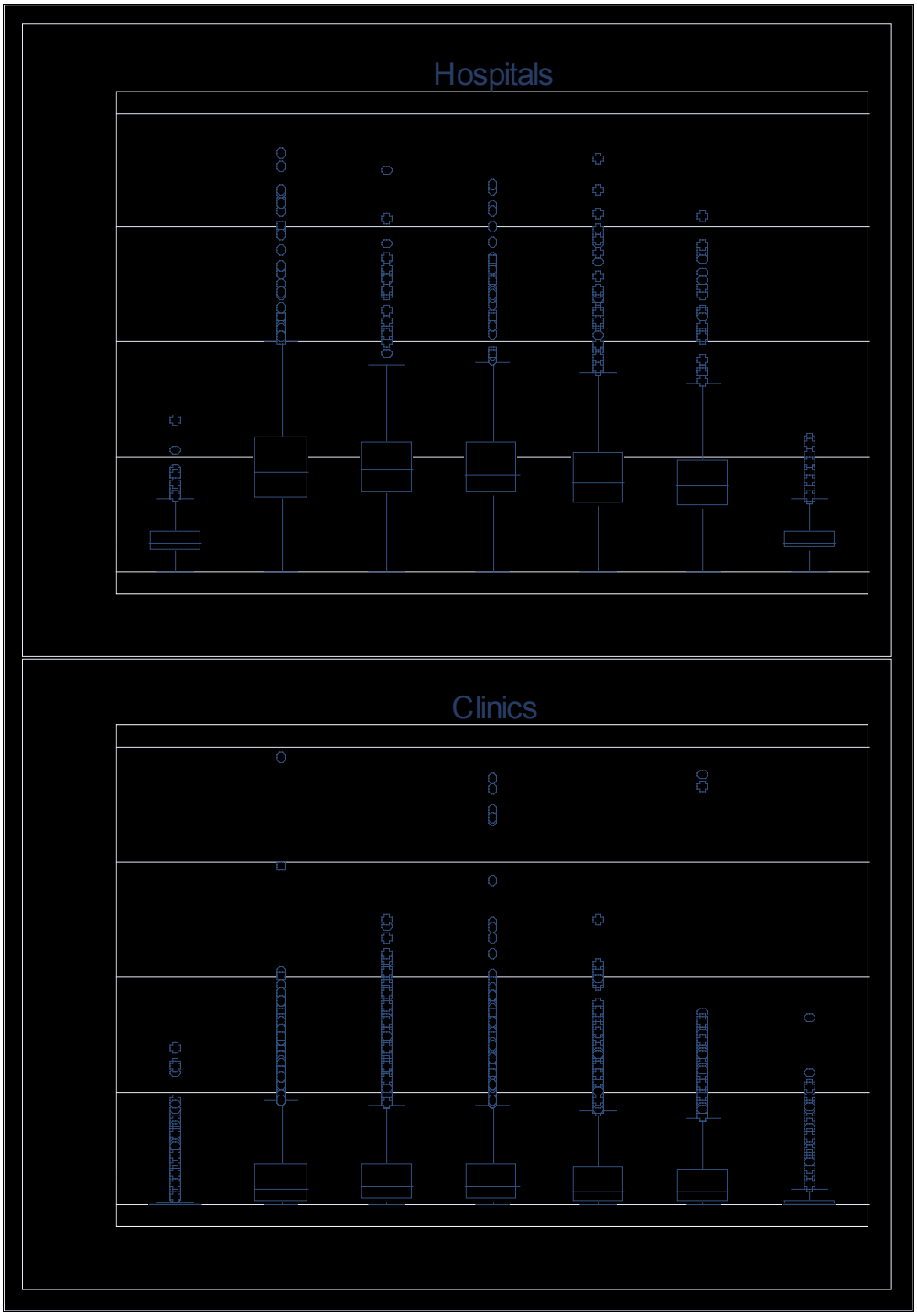


Figure 4.1: Day-of-the-week effect in laboratory test orders

Time series correlations among series with similar day-of-the-week effects are likely to be high because some of the correlation may be due to the day-of-the-week

effect rather than to actual changes in disease patterns. For example, in the National Capital area (NCA), the time series correlation between stool cultures and respiratory diagnoses is 0.57 when calculated on the raw data and less than 0.01 when the day-of-the week effect is removed. Similarly, the correlation between throat cultures and GI diagnoses is 0.80 when calculated on the raw data and 0.47 when the day-of-the-week effect is removed. (Day-of-the-week effects were removed by calculating seven-day moving averages, as described below.)

The time series should be corrected for day-of-the-week effects in order to focus specifically on changes due to disease patterns rather than changes due to weekly cycles. To remove the weekly cycle we calculated 7-day centered moving averages. The 7-day centered moving average for a particular day is defined as the arithmetic mean of the counts on the current day, the three previous days, and the three following days.

It is possible for two related time series to have a low correlation if one of the series lags behind the other. For example, if patients diagnosed with GI illness are typically asked to return for a second visit three days after the first, and only give a stool sample after the second visit, then the time series for GI syndrome and stool culture will be correlated with a three-day lag. This relationship would not be observed if correlations were only calculated between syndrome counts and laboratory tests on the same day. We examined correlations between syndrome/laboratory test pairs for the same day, after lagging syndrome counts by up to six days, and after lagging laboratory test counts up to six days. The highest of these 13 correlations was selected as best describing the relationship between the syndrome/laboratory test pair.

In 25 percent of the syndrome/laboratory test pairs, the laboratory test time series did not lead or lag behind the syndrome time series. The syndrome series lagged behind the laboratory test series 37 percent of the time, and the laboratory test series lagged behind the syndrome series 37 percent of the time. These results suggest that there is no overall advantage to one data source or the other with respect to timeliness. However, for particular syndromes and regions, one data source may provide an earlier indication of changes in disease patterns.

Eighteen percent of the syndrome/laboratory test pairs in the six selected regions had time series correlations greater than 0.2. Associations are listed in Table 4.4. These correlations were further compared with the CDC expert panel's laboratory test/syndrome associations. Results are described below.Table 4.4: Tests associated with each syndrome, based on criterion of correlation >0.2 in at least one region

Botulism-like illness syndrome

The time series correlations generally support the CDC expert panel's suggestion that no laboratory tests are expected to be associated with the botulism-like illness syndrome. All correlations with this syndrome were less than 0.5. Among the tests most correlated with this syndrome were urine cultures ($r = 0.45$ in San Diego and $r = 0.27$ in Hawaii). Urine cultures are the most commonly ordered test overall, so this association may simply reflect frequency of outpatient visits. Some tests for sexually transmitted infections may be associated with botulism-like illness visits; the correlation with Chlamydia cultures at Ft. Benning was 0.28 and the correlation with other STIs in the NCA was 0.48.

Table 4.4: Tests associated with each syndrome, based on criterion of correlation >0.2 in at least one region

Bot_like	Fever	GI	Hemr_ill
OTHER_STD	THR_CULT	THR_CULT	UA_CULT
UA_CULT	VIRAL_CULT	GC_CULT_SMEAR	BLD_PARA
O___P	GROUP_A_STREP	UA_CULT	FUNGUS__GENITAL
RESP_CULT	GC_CULT_SMEAR	GROUP_A_STREP	OTHER_STD
WND_CULT	SPUTUM_CULT	LEISHMANIASIS	GENITAL_CULTURE
GROUP_B_STREP	CHLAMYDIA_CULT	INFLUENZA	CHLAMYDIA_CULT
STOOL_CULT	BLD_CULT	FOB	CSF_CULTURE
FUNGUS__CSF	AER_BLD_CULT	GENITAL_CULTURE	GC_CULT_SMEAR
MISC_CULTURE	STOOL_CULT	OTHER_STD	VIRAL_CULT
FUNGUS__OTHER	INFLUENZA	H_PYLORI_CULT	GROUP_B_STREP
GENITAL_CULTURE	GRAM_STAIN	STOOL_CULT	NASAL_CULT
FUNGUS__RESP	AFB	FUNGUS__OTHER	FUNGUS__CSF
CHLAMYDIA_CULT	EYE_CULT	FUNGUS__GENITAL	O___P
BLD_PARA	FUNGUS__CSF	FECAL_WBC	ANAER_CULT
FOB	FOB	RSV	FUNGUS__OTHER
GC_CULT_SMEAR	RESP_CULT	O___P	MRSA
AFB	UA_CULT	NASAL_CULT	FOB
SPUTUM_CULT	BLD_PARA	BRUCELLA_CULT	ANAER_BLD_CULT
PINWORM	OTHER	RESP_CULT	STOOL_CULT
THR_CULT	RSV	AFB	THR_CULT
GRAM_STAIN	GENITAL_CULTURE	OTHER_GI	ACINETOBACTER
FUNGUS__GENITAL	VARICELLA	WND_CULT	LEISHMANIASIS
		SPUTUM_CULT	GRAM_STAIN
		ANAER_CULT	OTHER
		VARICELLA	AEROBIC_CULT
		HERPES	BF_CULT
		EYE_CULT	RESP_CULT
		PAP_SMEAR	SPUTUM_CULT
			BRUCELLA_CULT

Neuro	Rash	Resp	Shk_Coma
FUNGUS__GENITAL	GROUP_B_STREP	THR_CULT	GROUP_B_STREP
OTHER_STD	UA_CULT	GROUP_A_STREP	MRSA
UA_CULT	ANAER_CULT	VIRAL_CULT	ANAER_CULT
EYE_CULT	O___P	GC_CULT_SMEAR	O___P
H_PYLORI_CULT	GC_CULT_SMEAR	INFLUENZA	FUNGUS__GENITAL
FUNGUS__OTHER	OTHER_STD	BLD_CULT	LEGIONELLA_CUL
GENITAL_CULTURE	WND_CULT	RESP_CULT	GRAM_STAIN
OTHER	FUNGUS__OTHER	AFB	BF_CULT
GROUP_B_STREP	MRSA	RSV	RESP_CULT
WND_CULT	BF_CULT	UA_CULT	FUNGUS__OTHER
CHLAMYDIA_CULT	AFB	FOB	WND_CULT
ACINETOBACTER	GRAM_STAIN	SPUTUM_CULT	SPUTUM_CULT
BLD_PARA	FUNGUS__RESP	CHLAMYDIA_CULT	UA_CULT
CSF_CULTURE	THR_CULT	GENITAL_CULTURE	OTHER_GI
MISC_CULTURE	OTHER	EYE_CULT	GC_CULT_SMEAR_
AEROBIC_CULT		GRAM_STAIN	BLD_CULT
AER_BLD_CULT		BORDETELLA_CUL	BLD_PARA
PINWORM		OTHER_GI	CHLAMYDIA_CULT
BRUCELLA_CULT		FUNGUS__CSF	
		AER_BLD_CULT	
		NASAL_CULT	
		CSF_CULTURE	
		STOOL_CULT	
		HERPES	

Fever syndrome

The CDC expert panel associated blood, viral and MRSA cultures and Gram stains with the fever syndrome. This study found no association between fever visits and MRSA tests, and a slight association between fever visits and Gram stains in one region ($r = 0.33$ in San Diego). Blood cultures showed the highest association with fever diagnoses, with correlations greater than 0.2 in all regions. Correlations range from 0.27 in Hawaii to 0.44 in the NCA. Viral cultures were strongly associated with fevers in two of the six regions ($r = 0.61$ in Hawaii, $r = 0.72$ in the NCA). San Diego did not report any viral cultures during this period.

Throat cultures are highly correlated with the fever syndrome. Correlations were greater than 0.6 in all regions except San Diego, where the correlation was 0.23. Group A strep was highly correlated with fevers in the NCA ($r = 0.67$) and at Wright-Patterson ($r = 0.62$). These findings suggest considerable overlap between the fever and respiratory syndromes.

Gastrointestinal syndrome

Time series correlations with the GI syndrome were uniformly low. The strongest correlation was with throat cultures in Hawaii ($r = 0.63$). Stool cultures were moderately correlated with GI illness in all regions, with correlations ranging from 0.25 in San Diego to 0.39 in the NCA. Other GI tests identified by the CDC expert panel that had correlations of at least 0.2 with GI illness in at least one region are fecal white blood cells, fecal occult blood, H. pylori, and ova and parasites. C. difficile, E. coli, fecal reducing substances, Giardia/crypto, rotavirus, vibrio, yersinia, and salmonella/shigella/campylobacter tests were associated with GI illness by the CDC

expert panel but were not correlated with GI syndrome diagnoses in this analysis. All of these tests are ordered infrequently, so the basis for estimating these correlations is weak. Finally, the time series analysis identified an association between GI illness and Group A strep that was not identified by the CDC panel (r = 0.51 in the NCA, and r = 0.53 at Wright-Patterson AFB).

Hemorrhagic illness syndrome

The time series correlations generally support the CDC expert panel's suggestion that no laboratory tests are expected to be associated with the hemorrhagic illness syndrome. All correlations with this syndrome were less than 0.6. Among the tests most correlated with this syndrome were urine cultures (r = 0.40 in Hawaii and r = 0.56 in the NCA). As noted for the botulism-like illness syndrome, urine cultures are the most commonly ordered test overall, so this association may simply reflect increased frequency of visits to healthcare providers who then order standard tests. Other moderate correlations with hemorrhagic illness include blood parasite tests (r = 0.47 at Ft. Benning), genital fungus tests (r = 0.46 in Hawaii) and other STIs (r = 0.41 in the NCA).

Neurological illness syndrome

Neurological illness is a rare syndrome, with fewer than 5,000 diagnoses in the six selected regions over a two-year period (fever, by comparison, was diagnosed nearly 142,000 times). None of the correlations with neurological illness exceeded 0.5, perhaps because of the infrequent diagnosis. The CDC expert panel identified cerebrospinal fluid (CSF) cultures as associated with neurological illness, and this is somewhat confirmed in the time series analysis. Three of the six regions showed correlations between neurological illness and CSF culture exceeding 2.0 (r = 0.28 in Hawaii, r = 0.23 in

Pensacola, r = 0.30 in San Diego). There were several other tests with correlations between 0.2 and 0.5, but no consistent patterns.

Rash syndrome

The CDC expert panel associated skin, viral, and wound cultures, and herpes and varicella tests, with rash syndrome. Of these associations, only wound cultures is confirmed by the time series analysis, and even then the association is only observed in the NCA (r = 0.35) and San Diego (r = 0.34). Other notable correlations were with MRSA (r = 0.30 in the NCA), fungus tests (r = 0.31 in the NCA and r = 0.29 in San Diego), group B strep (r = 0.53 in the NCA and r = 0.44 in San Diego), and anaerobic cultures (r = 0.45 in the NCA and r = 0.31 in San Diego).

Respiratory syndrome

Throat cultures were correlated with respiratory syndrome diagnoses in all six regions. Correlations ranged from 0.35 in San Diego to 0.85 in Pensacola, and exceeded 0.8 in four out of five regions. In San Diego, the highest correlation with respiratory illness was for respiratory cultures (r = 0.43) rather than throat cultures (r = 0.35). It is likely that this represents a difference in terminology among regions rather than a difference in medical practice.

Tests for group A strep were strongly associated with respiratory illness in two regions (r = 0.77 in the NCA and r = 0.72 at Wright-Patterson), but this correlation was less than 0.2 in the other four regions. Similarly, viral cultures were strongly associated with respiratory illness in the NCA (r = 0.67) but not in the other regions (r = 0.24 in Hawaii, and r < 0.2 in the other four regions).

The CDC expert panel associated several more specific tests with the respiratory syndrome. Four of these associations (Bordetella pertussis, Chlamydia, influenza and RSV) were identified for at least one region in the time series analysis, while the rest (AFB, Brucella, respiratory fungus, Gram stains, Legionella, and mycoplasma) were not. Blood cultures were associated with respiratory illness in the time series analysis, but not by the CDC expert panel; correlations ranging from 0.24 to 0.44 were observed in all six regions.

Shock/coma syndrome

No correlations with the shock/coma syndrome exceeded 0.6. This is a rare syndrome, with only 2,105 diagnoses in the five regions during the two-year period. One interesting finding for this syndrome, however, is that the correlation with ova/parasite tests exceeded 0.2 for two regions ($r = 0.22$ in Hawaii, $r = 0.36$ in the NCA). This is consistent with the finding that ova and parasite exams are three times more likely to be ordered in conjunction with a shock/coma syndrome diagnosis than would be expected by chance.

In summary, the associations identified under this criterion are similar to the associations proposed by the CDC expert panel, but very few correlations exceeded 0.6. The strongest correlations, not surprisingly, are with respiratory illness, a high-volume syndrome with a strong seasonal pattern. A few associations that were not suggested by the CDC expert panel, such as MRSA and rash, blood cultures and respiratory illness, and group A strep and fever, should be considered further for surveillance.

Criterion #3: Outbreak peaks

The final criterion for associating laboratory tests with syndromes is signal-to-noise ratio during outbreaks. A laboratory test is considered to be associated with a disease syndrome if orders exceed the usual volume by at least two standard deviations during an outbreak of the disease syndrome. The signal-to-noise ratio (SNR) is defined as

(peak count-mean count)/standard deviation (SD) of counts

where the mean and standard deviation of counts are calculated during a baseline period preceding the outbreak, and the peak count is defined as the maximum daily count observed during the defined outbreak period. Seven-day moving averages are used rather than raw counts in order to eliminate the day-of-the-week effect. This criterion was used by researchers from WRAIR and the Johns Hopkins University Applied Physics Lab (JHU/APL) in their evaluation of the BioNet disease surveillance system in San Diego, California[64].

Signal-to-noise ratios are calculated during verified outbreaks. Most such outbreaks are for respiratory and gastrointestinal illnesses. The evaluation of the BioNet program focused on three outbreaks in San Diego: the October 2003 wildfires, the influenza season of 2003-2004, and an outbreak of suspected norovirus at the Marine Corps Recruit Depot in early 2004. This study will focus on the same outbreaks for comparability. In addition we will consider the 2003-2004 influenza season in the NCA, in order to explore regional differences in test ordering patterns during outbreaks.

San Diego Wildfires

Johnson et al. describe the wildfires in their article, "Leveraging Syndromic Surveillance During the San Diego Wildfires, 2003" [65]:

> "On October 25, 2003, one of the largest fires in California history began in San Diego County. Over a period of three days, the air quality deteriorated to unhealthy and hazardous levels, prompting school cancellations and the general public to stay at home."

During this event, the authors monitored ambulance calls, emergency department visits, and over-the-counter medication sales, and observed increases in respiratory indicators including asthma-related emergency department visits and local sales of respiratory medications. The BioNet evaluation team found in addition that outpatient visits to MTFs for asthma-related conditions increased during this event.

Examination of SNRs for each laboratory test during October 2003 identified only one laboratory test, tissue cultures, with a SNR greater than two during the wildfire event. However, examination of a time series plot of tissue cultures suggests that this peak is part of an increase in tissue cultures beginning in late September, so it is likely unrelated to the wildfires. Even during this peak, there were generally no more than one or two tissue cultures ordered per day in the San Diego region. The laboratory test data may not be the best data source for tracking the health consequences of this event. This is not surprising since microbiology lab tests are expected to be ordered more often in the presence of an infectious disease, and the wildfires represent exposure to irritants in the environment.

Annual influenza

Several laboratory tests peaked strongly during the 2003-2004 influenza season in San Diego (Figure 4.2a). Throat cultures showed the strongest association, with a SNR of 7.60 (compared with a SNR of 5.03 for respiratory diagnoses), and a peak eight days before the peak for respiratory diagnoses. Throat cultures also show several peaks during the summer and fall of 2003; it is unclear whether these represent true outbreaks or random variability.

The SNR for respiratory cultures was 6.57 during influenza season, but respiratory cultures lagged behind other indicators of influenza, with a peak in early January. Blood cultures showed a peak SNR of 3.31 but did not peak until after respiratory visits. Gram stains showed a peak SNR of 6.2 one day before the peak for respiratory diagnoses, but also show several additional peaks in the fall so may not be the most specific indicator of the influenza season (data not shown).

Throat, respiratory and blood cultures also peaked in the NCA during the 2003-2004 influenza season (figure 4.2b). Throat cultures track very closely with respiratory visits and show a similar peak SNR (3.76, compared with 4.38 for respiratory visits). Respiratory cultures increased slightly during influenza season, with a short peak in early December and a max SNR of 2.73. Blood cultures showed a higher peak (SNR = 8.26). The strongest signal in the NCA was for viral cultures, which were not ordered at all in San Diego. The SNR was 27.10,. The SNR for viral cultures first exceeded 2.0 a day earlier than the SNR for respiratory visits, and the SNR for viral cultures stayed elevated throughout influenza season. The significance of viral cultures in the NCA, when no tests were reported by this name in San Diego, illustrates the importance of regional differences in test ordering patterns.

Gastrointestinal outbreak at MCRD San Diego

An outbreak of suspected norovirus occurred in the San Diego region in January 2004. Outpatient visits for gastrointestinal illness were elevated for two months, with a SNR of 18.45 on January 15th. Several laboratory tests also increased during this outbreak: fecal white blood cells peaked on January 17th, with a SNR of 3.60, and stool cultures peaked on January 18th with a SNR of 3.69. Both of these tests showed lower SNRs and later peaks than outpatient visits for gastrointestinal illness, so it is not clear whether laboratory tests can improve surveillance for this syndrome. The association of these two tests with the outbreak is promising, however, since laboratory data may be available for surveillance in a more timely fashion than outpatient visit data.

Other laboratory tests associated with this outbreak include fecal occult blood tests (SNR 3.65, peak February 1) and pinworms (SNR 4.92, peak January 26). Both of these tests show a markedly later outbreak signal than outpatient visits, so they may not be useful for detecting outbreaks. However, they may still be useful for monitoring outbreaks. Finally, genital cultures (SNR 4.04, peak January 17) and Gram stains (SNR

5.61, peak January 10) increased during this outbreak.

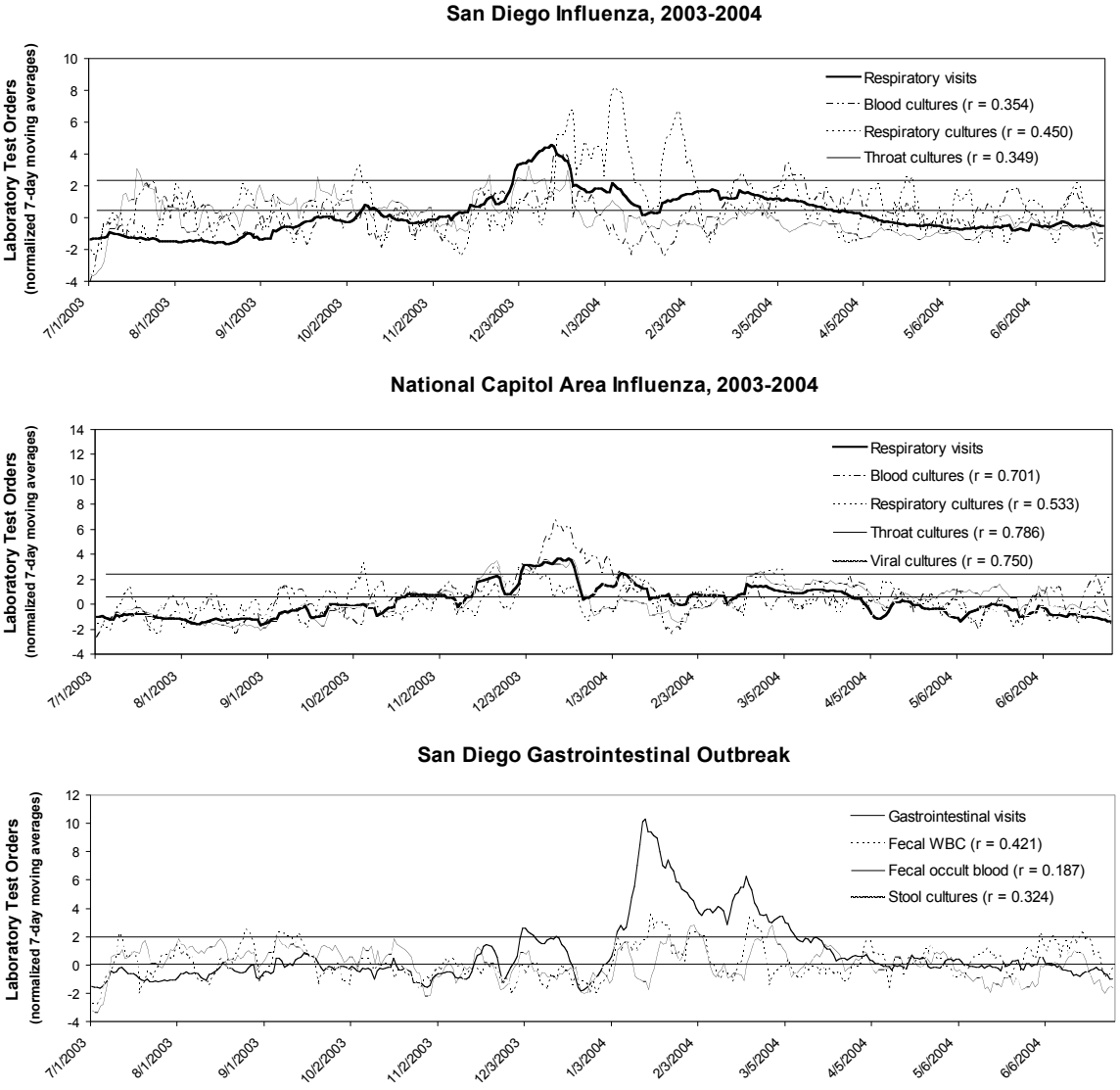


Figure 4.2: Patterns of laboratory test ordering during known outbreaks

In summary, this criterion identified a subset of laboratory tests that were associated with respiratory and gastrointestinal illness under the first two criteria, that also increased during influenza and suspected norovirus outbreaks, respectively. Different laboratory tests were associated with influenza in different regions,

underscoring the importance of understanding regional health care variations when using electronic records for disease surveillance.

Discussion and recommendations

The goal of this analysis is to identify laboratory tests that might be useful for disease surveillance. Based on our results, we propose for surveillance the five syndrome groups listed in table 4.5. These groups correspond closely to those proposed by the CDC expert panel; differences are discussed below.

Fever syndrome

Anaerobic and aerobic cultures are not included in our list but are included on the CDC list. The CDC list does not distinguish between aerobic and anaerobic cultures of blood and other body fluids. The DoD data allow this distinction, and only blood cultures are associated with fever in the DoD data. The CDC list includes MRSA tests under the fever syndrome, but we found a stronger association between MRSA and rash. Group A strep tests showed a strong association with fever syndrome in our analysis but we chose instead to include these tests in the respiratory syndrome as proposed by the CDC.

Gastrointestinal syndrome

All tests proposed by the CDC expert panel were confirmed by criterion #1 and included on our list. The other criteria confirmed only fecal WBC, fecal occult blood, ova/parasites and stool cultures, probably because the other tests are ordered rarely, or are ordered as part of a generic stool culture rather than by name.

Neurological syndrome

This syndrome includes only CSF cultures and CSF fungus tests, as proposed by the CDC panel. Our analysis identified other associated tests, including other fungus, Gram stains, herpes, varicella, and viral cultures. All of these tests are associated with other syndromes in addition to neurological, and may not be specific to neurological illness.

Rash syndrome

Our analysis confirmed the associations identified by the CDC expert panel, along with anaerobic cultures, other fungus, and MRSA. Anaerobic cultures were identified by both criteria #1 and #2, and specimens for these cultures tended to be skin and wounds. Other fungus is not a category in the CDC laboratory data. Specimens for this test are mostly skin and nails.

Respiratory syndrome

Several tests identified by the CDC expert panel were not associated with respiratory illness in this analysis: acid-fast bacilli (AFB), Brucella, respiratory fungus, Legionella, and Mycoplasma. AFB may reflect chronic illness, and the others are rarely ordered. If they were included in this syndrome it is likely that these rare tests would disappear in the "noise" of throat, respiratory and viral cultures. If the rare tests are of specific interest they should be monitored separately from respiratory syndrome.

Table 4.5: Proposed syndrome grouping for microbiology laboratory tests

Bot_like	Fever	GI	Hemr_ill
NONE	AER BLD CULT ANAER BLD CULT BLD CULT BLD PARA GRAM STAIN VIRAL CULT	C DIFFICILE E COLI O157:H7 FECAL RS FECAL WBC FOB GIARDIA/CRYPTO H PYLORI CULT O & P OTHER GI ROTAVIRUS SSC STOOL CULT VIBRIO YERSINIA CULT	NONE
Neuro	**Rash**	**Resp**	**Shk_Coma**
CSF CULTURE FUNGUS, CSF	ANAER CULT FUNGUS, OTHER HERPES MRSA VARICELLA WND CULT	BORDETELLA CULT CHLAMYDIA CULT GROUP A STREP INFLUENZA RESP CULTURE RSV THR CULT VIRAL CULT	NONE

Syndrome associations

Once the final syndrome definitions were developed, criteria #1 and #2 were revisited to confirm that once tests were combined into a syndrome, tests associated with a syndrome were more likely to be ordered during visits for the syndrome, and daily counts of all tests in a syndrome are correlated over time with outpatient visits for the syndrome. Table 4.6 shows that observed/expected ratios and correlations were generally strong between laboratory test-based syndromes and outpatient visit-based syndromes. Observed/expected ratios were all greater than 3.0 and correlations exceeded 2.0 for three of five syndromes. The neurological syndrome had a relatively weak time series

correlation between the two data sources, probably because daily counts are so low, but had the highest observed/expected ratio, because neurological tests are rarely ordered in the absence of a diagnosis of neurological syndrome. The rash syndrome showed the weakest overall association based on both criteria. This may be driven by the wound cultures, which are as likely to be associated with a fever diagnosis as with a rash. The definition of the rash syndrome could be revisited in the future depending on what patterns are seen in prospective surveillance.

Table 4.6: Association between laboratory and ICD-9 syndromes

	Observed/Expected ratio	Median correlation
Fever	16.42	0.375
GI	14.91	0.290
Neuro	468.90	0.179
Rash	3.64	0.146
Resp	7.28	0.815

Further recommendations

In addition to identifying syndrome groups, this analysis identified several other issues important to using laboratory tests for surveillance:

- Laboratory tests are currently archived only after the test result is certified, even though test ordering information is entered electronically at the time of order. In order for laboratory test data to provide timely indicators of disease patterns, the electronic data collection system should be modified to monitor laboratory tests as they are ordered.
- Laboratory test names should be standardized to facilitate consistent monitoring across MTFs and over time. Standard laboratory test terminology, such as

LOINC and SNOMED coding, is used in other systems and is being evaluated for the laboratory module of CHCS II [66]. DoD epidemiologists may wish to participate in the development of the laboratory module of CHCS II, to ensure that the data are collected in such a way that they may ultimately be used for surveillance.

- Our test name standardization method is ad hoc and would need to be updated every time a new spelling is observed. If routine surveillance of laboratory test orders is implemented before test names are standardized, it would be useful to employ a text extraction algorithm that could "recognize" alternate spellings of the same test name. The standard test list developed for this project could be used as a starting point to train the text extraction algorithm.
- Monitoring laboratory tests grouped into broad syndrome categories may be useful for detecting influenza or many gastrointestinal illness outbreaks, but is likely to miss small to medium sized outbreaks of rare illness. Laboratory tests for diseases of specific interest should be monitored independently of the syndrome groups.
- Blood cultures are associated with all five major syndromes, and do not appear to be indicators of any specific illness. Blood cultures could be monitored separately as an indicator of the overall level of severe infectious disease in a population.
- Laboratory test monitoring may be most useful at the hospital or regional level. Clinics tended to order only about seven total tests per day, and many (if not most) of these were routine (e.g. urine cultures). Under regional surveillance, if

increases are noted in a region, it might be possible to drill down through the data and see if they were all ordered in the same hospital or clinic.

In summary, outpatient visit data have been shown to be a useful data source for syndromic surveillance. Laboratory tests are associated with both outpatient visit data and with disease outbreaks, suggesting that laboratory tests are a valid indicator of disease patterns in the population. We will further evaluate the proposed syndrome groupings for laboratory tests in the next chapter.

CHAPTER V: Evaluating outbreak detection performance

Introduction

The second specific aim of this study is to evaluate strategies for using laboratory test orders for syndromic surveillance, alone and in combination with outpatient visit data. The evaluation will focus primarily on the respiratory and gastrointestinal syndromes, since several naturally-occurring outbreaks have been identified during the time frame of the study for these syndromes. This chapter will describe the data, outbreaks and surveillance algorithms used to evaluate the laboratory data; describe the sensitivity, specificity, and timeliness of outbreak detection based on laboratory test order data for respiratory and GI syndromes; and present case studies illustrating surveillance for fever, neurological, and rash syndromes.

Description of data

Daily counts of laboratory test orders and outpatient visits are used for this analysis. These data sets are described in detail in Chapter 4. In brief, data from November 2002 through November 2004 were aggregated by data source, day, syndrome and region, resulting in a file with daily counts of outpatient microbiology laboratory tests for each syndrome and region, and daily counts of outpatient visits to MTFs for each syndrome and region. Syndromes considered include fever, gastrointestinal, neurological, rash, and respiratory. Laboratory tests associated with each syndrome are listed in chapter 4, and outpatient visit diagnoses associated with each syndrome are listed in Appendix 3.

Outbreaks

The evaluation of outbreak detection performance is limited by the availability of only two years of historical data containing a limited number of documented outbreaks. Evaluation using the same data that was used for developing the syndrome definitions could result in biased estimates of outbreak detection performance. Specifically, in Chapter 4, we examined four known outbreaks in two regions to identify laboratory tests that increased during the outbreaks. Since we defined the laboratory gastrointestinal and respiratory syndromes in part by identifying laboratory tests that increased during those outbreaks, by definition laboratory test orders for the syndromes must increase during those outbreaks. To obtain a valid test of outbreak detection, we examine whether laboratory test orders for the syndromes increased during different outbreaks and in different regions.

For this analysis we focus on outbreaks that were identified for the Defense Advanced Research Projects Agency (DARPA) Five Cities Evaluation[61, 63]. These outbreaks were identified by an expert panel made up of epidemiologists from several syndromic surveillance research teams. The panel examined multiple syndromic surveillance data sources, including visits to outpatient military treatment facilities, but they did not have access to laboratory test order data. Panel members examined daily counts both visually and using a simple anomaly detection algorithm, and after discussion came to consensus regarding dates and locations of outbreaks. They jointly identified for each outbreak the likely start date, peak date, end date, and date at which public health officials would have been likely to respond (PH date). They were able to confirm a few of the outbreaks they identified using traditional surveillance methods. Six of the

outbreaks identified by the expert panel took place at times and sites covered by the retrospective laboratory order data; these outbreaks are used in this evaluation. Dates and locations of these outbreaks are listed in table 5.1, and daily counts are plotted in figures 5.1 and 5.2. Note that laboratory test order data are available beginning in November 2002, so only three days of baseline data are available for the Pensacola respiratory outbreak that began on November 4, 2002. After checking for differences in baseline rates, we used data from November 2004 to "train" the detection algorithms to detect the Pensacola respiratory outbreak.

Table 5.1: DARPA-identified outbreaks

Syndrome	**City**	**Start date**	**PH date**	**Peak date**	**End date**
Respiratory	Charleston	27-Jan	3-Feb	10-Feb	19-Mar
	Pensacola	4-Nov	10-Dec	3-Feb	14-Apr
	Norfolk	3-Feb	18-Feb	24-Feb	15-Apr
Gastrointestinal	Charleston	6-Dec	18-Dec	17-Dec	28-Jan
	Norfolk	11-Nov	9-Dec	24-Feb	16-Apr
	Norfolk	22-Feb	24-Feb	24-Feb	11-Mar

Surveillance algorithms

This analysis primarily uses the DoD-ESSENCE algorithm in order to make the results of the study most relevant for DoD-ESSENCE planners in the future. As described above, this algorithm uses a regression model (useful for large daily counts) but switches to a simple EWMA algorithm when the regression model does not fit well (usually when daily counts are low). For comparison purposes we explored the EARS C1 and C3 algorithms[67] based on CUSUM methodology, a stand-alone EWMA algorithm[56], and a temporal scanning algorithm[68]. The DoD-ESSENCE algorithm was run using SAS code obtained from DoD-ESSENCE statistical programmers, and the comparison algorithms were run using an Excel program provided by Howard Burkom of

the Johns Hopkins University Applied Physics Lab[69]. These algorithms are described in Chapter 2.

In general, as the threshold for alerting is raised, false alarms will be less frequent (increased specificity) but smaller outbreaks are more likely to be missed (decreased sensitivity) and outbreaks will be caught later in their development (decreased timeliness). To evaluate tradeoffs among sensitivity, specificity and timeliness, we chose four different background alerting rates (specificities) and report sensitivity (proportion of outbreaks detected before the PH date) and timeliness for each background alerting rate. We report background alerting rates rather than true specificities because we do not know for sure whether an outbreak exists on any particular day. It is impossible to obtain the true specificity of the detection algorithm in this framework. The background alerting rate is calculated as the number of alerts (excluding the known outbreak) divided by the number of days (excluding the known outbreak). Timeliness is defined as the median number of days from outbreak start date to first alert during the outbreak period. Outbreak periods that had no alerts were counted as censored (time to alert greater than length of outbreak) when calculating medians.

We also plot modified ROC (receiver operating characteristic) curves, with number of outbreaks detected on the vertical axis and estimated background alerting rate on the horizontal axis (figures 5.3 and 5.4). This allows comparison of different algorithms and/or data sources across a range of background alerting rates.

Combining data sources

Laboratory test order data are not expected to replace outpatient visit data in ESSENCE, but to augment them. We explored a simple method for evaluating the

laboratory test order data in combination with outpatient visit data to investigate whether combining the data sources increases the signal-to-noise ratio in the data. The DoD-ESSENCE algorithm yields *p*-values for each data stream indicating the likelihood of a daily count at least as extreme as the observed count if no outbreak is ongoing, These separate *p*-values are combined to obtain a composite *p*-value comparing observed events to expected events. The methods of Edgington [54] and Fisher [53], described in Chapter 2, are adapted for this analysis. Neither is likely to be implemented in ESSENCE; the purpose of using these methods for this analysis is to quantify in a simple way the added value of the laboratory test order data. In practice, when laboratory test order data are first incorporated into DoD-ESSENCE it is likely to be as an informal check or confirmation of the patterns observed in the outpatient visit data. Long range plans may include Bayesian models for combining multiple data sources.

The methods of Edgington and Fisher involve additive and multiplicative functions of *p*-values from separate data streams. The authors describe a parametric methodology for determining the significance of these functions. In this analysis, it would be inappropriate to assume that the laboratory test order data and outpatient visit data are independent data streams, since laboratory tests are almost always ordered in conjunction with an outpatient visit. However, without specifying a covariance structure for the two data streams or a distribution for the sums and products of *p*-values, it is still possible to identify increases above baseline. In this analysis we use historical data to estimate thresholds for alerting that will yield background alerting rates of one per two weeks, one per four weeks, one per six weeks, and one per eight weeks, and examine the sensitivity and timeliness of the combined p-values.

Evaluation results

Daily counts of respiratory and gastrointestinal laboratory tests and outpatient visits in outbreak sites were analyzed using the DoD-ESSENCE algorithm. For respiratory outbreaks, DoD-ESSENCE alerted before the PH date in all three outbreaks and both data sources (figure 5.1). Each data source alerted during one of the three gastrointestinal outbreaks, but not during the same outbreak (figure 5.2). This suggests the possibility that laboratory tests and outpatient visits may complement each other by detecting different types of outbreaks.

The DoD-ESSENCE algorithm alerts when the p-value comparing observed to expected counts exceeds 0.995. For direct comparison of data sources and algorithms, the alerting threshold was modified empirically so the number of alerts excluding the outbreak period was exactly one per two, four, six, or eight weeks. Because of the modified thresholds, the results below do not match the alerts plotted in figures 5.1 and 5.2.

Comparison of data sources using the DoD-ESSENCE algorithm.

Laboratory test orders performed nearly as well as outpatient visits for detecting outbreaks in this data set (Table 5.2). At a background alerting rate of one alert every six weeks, using laboratory test order data, the DoD-ESSENCE algorithm was able to detect two out of three respiratory outbreaks prior to the public health recognition date, both on the first day of the outbreak. None of the three gastrointestinal outbreaks were detected prior to public health recognition date, although all of the three missed gastrointestinal outbreaks alerted before the end of the outbreak. Median timeliness for all outbreaks (including those detected after the PH date) was 17 days.

Table 5.2: Date of first alert, sensitivity (number of outbreaks detected) and timeliness (days from outbreak start date to first alert), DoD-ESSENCE algorithm.

	Outbreak dates		Date of first alert			
Outbreak	Start date	PH date	1/2wks	1/4wks	1/6wks	1/8wks
Laboratory test order data						
Resp-1	27-Jan	3-Feb	2-Feb	2-Feb	ND	ND
Resp-2	4-Nov	10-Dec	4-Nov	4-Nov	4-Nov	4-Nov
Resp-3	3-Feb	18-Feb	3-Feb	3-Feb	3-Feb	3-Feb
GI-4	6-Dec	18-Dec	6-Jan	7-Jan	7-Jan	7-Jan
GI-5	11-Nov	9-Dec	11-Nov	11-Nov	13-Jan	13-Jan
GI-6	22-Feb	24-Feb	23-Feb	24-Feb	24-Feb	24-Feb
No. detected before PH date			5/6	4/6	2/6	2/6
Median timeliness			0.5	1	17	17
Outpatient visit data						
Resp-1	27-Jan	3-Feb	28-Jan	28-Jan	1-Feb	1-Feb
Resp-2	4-Nov	10-Dec	4-Nov	4-Nov	4-Nov	ND
Resp-3	3-Feb	18-Feb	3-Feb	3-Feb	ND	ND
GI-4	6-Dec	18-Dec	9-Dec	9-Dec	9-Dec	9-Dec
GI-5	11-Nov	9-Dec	12-Nov	7-Dec	7-Dec	7-Dec
GI-6	22-Feb	24-Feb	22-Feb	ND	ND	ND
No. detected before PH date			6/6	5/6	4/6	3/6
Median timeliness			.5	2	15	>26

ND, not detected (no alerts between outbreak start date and end date)

Using outpatient visit data, two of three respiratory outbreaks and two of three gastrointestinal outbreaks were detected before the public health recognition date. These four outbreaks were detected a median of four days after the outbreak start. Median timeliness for all outbreaks was 15 days. Figure 5.3 illustrates the tradeoff between outbreak detection (sensitivity) and background alerting rate (proxy for specificity). The line corresponding to the outpatient visit data lies slightly above the line for the laboratory test order data for background alerting rates below 1 per 10 weeks, indicating that at typical background alerting rates, more outbreaks are likely to be detected using the outpatient visit data.

A few interesting patterns were noticed with respect to specific outbreaks. During the Charleston gastrointestinal outbreak that began on 6 December, laboratory test orders "bottomed out" for several days, suggesting that possibly once the outbreak was identified, clinicians stopped ordering stool cultures. If this pattern is noticed during future outbreaks, it might be worth considering whether to modify the alerting algorithm to check for periods of unusually low counts as well as elevated counts. The brief, explosive outbreak in Norfolk in late February did not alert at all in the outpatient visit data, but alerted (albeit on the public health recognition date) in the laboratory test order data. So, while laboratory test order data may not perform as well overall as outpatient visit data, they may be useful for detecting or monitoring some outbreaks that are not recognized by existing syndromic surveillance.

Comparison of detection algorithms using laboratory test order data.

Although the DoD-ESSENCE algorithm performed reasonably well with the laboratory test order data, a simple EWMA algorithm may perform even better. Table 5.3 shows that at a background alerting rate of one alert every six weeks, the EWMA and SCAN algorithms detected more outbreaks (four of six) than the DoD-ESSENCE algorithm (two of six). The EWMA algorithm detected algorithms sooner than the other algorithms, with a median timeliness of 0.5 days. No single algorithm dominated the others with respect to the sensitivity/background alerting rate tradeoff (figure 5.2).

Table 5.3: Sensitivity and median timeliness, selected detection algorithms and background alerting rates, laboratory test order data.

Number of outbreaks detected before public health recognition date (out of six)				
Algorithm \ alerting rate	1/2wks	1/4wks	1/6wks	1/8wks
ESSENCE	5	4	2	2
EARS C1	6	5	3	3
EARS C3	5	4	3	2
EWMA	5	4	4	4
SCAN	4	4	4	3
Median timeliness (days from outbreak start to first alert)				
Algorithm \ alerting rate	1/2wks	1/4wks	1/6wks	1/8wks
ESSENCE	0.5	1.0	17.0	17.0
EARS C1	2.0	4.5	18.0	18.0
EARS C3	0.0	1.5	16.0	16.0
EWMA	0.0	0.5	0.5	1.0
SCAN	1.0	2.0	4.0	6.0

Note: median timeliness calculated for all outbreaks, including those not detected.

It is somewhat surprising that the EWMA algorithm performs better than the DoD-ESSENCE algorithm with laboratory test order data. The DoD-ESSENCE algorithm incorporates an EWMA component, which is used for alerting whenever the *r* squared value from the default regression model falls below a threshold. The DoD-ESSENCE regression model allows for weekly cycles and holiday clinic closings, patterns that are most pronounced in data sets with relatively large daily counts. Daily counts of laboratory test orders tend to be fairly small in most regions. For the three regions and the time frame discussed in this chapter, the median daily number of respiratory laboratory test orders was 21, and the median daily number of gastrointestinal test orders was only three. A priori, it seemed likely that the DoD-ESSENCE regression model would not fit the laboratory data well, and that most alerts would be triggered by the EWMA component of the algorithm. This is not the case, at least for respiratory outbreaks. The regression model was used for alerting 80 percent of the time. The comparison of methods suggests that if the EWMA component had been used more often, the detection performance might have been better. (For gastrointestinal laboratory test

orders, the regression model was used for alerting only seven percent of the time, in accordance with our original hypothesis.) It might be worthwhile to adjust the threshold for switching between regression and EWMA in the DoD-ESSENCE algorithm when using laboratory test data. Selecting an appropriate switching threshold would require more data and outbreaks to evaluate, and is beyond the scope of this dissertation.

Combining laboratory test order and outpatient visit data.

P-values for laboratory test counts were combined with *p*-values for outpatient visit counts as described above. At a background alerting rate of one per six weeks, surveillance based on combined data detected all three respiratory outbreaks before the PH date, and none of the GI outbreaks, although during the brief Norfolk outbreak the combined data alerted on the PH date. Therefore, sensitivity of the combined data (three outbreaks detected) fell between that of the laboratory data alone (two outbreaks detected) and the outpatient visit data alone (four outbreaks detected) (table 5.4). Combining p-values improved the timeliness of outbreak detection. Median time to first alert was more than two weeks when each data source was used alone, but was only four days when the data sources were combined. For three outbreaks, the combined data alerted on the earlier of the laboratory and outpatient visit alert dates, and for three outbreaks, the combined data alerted between the laboratory and outpatient visit alert dates. Combining data sources may be a promising strategy for early detection of respiratory and GI outbreaks.

Table 5.4: Sensitivity and median timeliness, data sources separate and combined.

Number of outbreaks detected before public health recognition date (out of six)				
Method \ alerting rate	1/2wks	1/4wks	1/6wks	1/8wks
Lab only (ESSENCE)	5	4	2	2
Outpatient visit only (ESSENCE)	6	5	4	3
Sum of p-values	4	3	3	3
Product of p-values	5	3	3	3
Median timeliness (days from outbreak start to first alert)				
Method \ alerting rate	1/2wks	1/4wks	1/6wks	1/8wks
Lab only (ESSENCE)	0.5	1.0	17.0	17.0
Outpatient visit only (ESSENCE)	0.5	2.0	15.0	>26
Sum of p-values	0.5	3.5	4.0	4.0
Product of p-values	0.0	3.5	4.0	4.0

Note: median timeliness calculated for all outbreaks, including those not detected.

Case studies: Fever, neurological, and rash syndromes

No known outbreaks have been identified during the period of this study for fever, neurological, and rash syndromes. Fever syndrome is observed to follow a seasonal pattern similar to the respiratory syndrome, so it can be evaluated with respect to detection of seasonal increases. Neurological and rash syndromes are much less common than the other syndromes, so even small increases in daily counts may signal an alert. To better describe the behavior of these syndromes in the absence of known outbreaks, we present case studies.

Rash syndrome. Both outpatient visits and laboratory tests for rash syndrome alerted in summer 2003 in San Diego (figure 5.5). An initial alert in laboratory tests on June 18 was followed by three consecutive alerts on July 8-10. These alerts corresponded to an increase in wound cultures. Three subsequent alerts on September 3-5 corresponded to an increase in MRSA tests. A single alert in outpatient visits was observed on June 27, nine days after the initial alert in laboratory test data. It is possible that these alerts represent a true MRSA outbreak; a documented MRSA outbreak

occurred in San Diego almost exactly one year prior in military recruits[70]. If so, the laboratory data provide an earlier and more sustained indication of the outbreak.

The national capital area also experienced an increase in laboratory tests and outpatient visits for rash in the summer of 2003 (figure 5.5). Outpatient visits for rash syndrome alerted first on June 3, while laboratory tests for rash syndrome alerted nearly a week later on June 9. Laboratory tests alerted again on July 2 and 9, and outpatient visits alerted on three additional days between August 25 and September 8. Laboratory test alerts corresponded to an increase in wound cultures with no corresponding or subsequent increase in MRSA tests, and it is unclear whether the increase is related to the San Diego outbreak.

While these increases do not occur during documented outbreaks, they suggest that laboratory test data can complement outpatient visit data for detecting and monitoring increases in rash syndrome. This is encouraging since rash tests are usually ordered during a visit that does not result in a diagnosis of rash; only 81 of more than 22,000 laboratory tests in the rash syndrome (0.36%) have a corresponding rash diagnosis recorded during an outpatient visit. Despite the lack of overlap between the two data sources, they both seem to capture these potentially important increases in San Diego and the National Capital area.

Neurological.

This syndrome was the least common, with average daily counts less than three for both outpatient visits and laboratory tests in all regions. A time series plot of outpatient visits with a neurological syndrome diagnosis in the national capital area shows what may be an outbreak beginning in August 2003, with an initial alert on August

18 and six more alerts up to and including the peak count of 15 on September 16 (figure 5.6). During this entire period, however, the daily number of laboratory tests for neurological syndrome never exceeded two.

At Camp LeJeune, the outpatient visit data for neurological syndrome show an increase in September 2004 with a single-day alert on September 21 (figure 5.6). Laboratory test orders for neurological syndrome alerted on September 2 and 3, nearly three weeks before the alert in the outpatient visit data. This may be an early indication for the second alert period noted in the outpatient visit data, or it may be unrelated. While laboratory test orders provide some corroboration for the observed increase in the outpatient visit data, they also have a higher background alerting rate than outpatient visits even though the significance level for alerting is set the same for both data streams. One possible explanation is neurological tests are often ordered in multiples. Of the 10,940 individuals in this data set for whom neurological tests were ordered, 5,430 (50%) had more than one neurological test ordered at the same MTF on the same day. Frequent combinations were CSF cultures and gram stains of the cerebrospinal fluid (n=3,387) and two separate CSF cultures (n = 1,660). This problem could be addressed by screening out multiple tests before applying the surveillance algorithm. Screening should be applied to all syndromes, but is unlikely to have much effect on syndromes other than neurologic because for other syndromes usually only one test in each syndrome is ordered per person at the same MTF on the same day.

Fever syndrome.

Fever data follow a seasonal pattern similar to that observed in respiratory data, perhaps because many winter fevers may be influenza-related. For this case study we

consider the winter 2003-2004 season in three regions: Camp LeJeune, San Diego, and the national capital area (Figure 5.7). Outpatient visits for fever in Camp LeJeune show a distinct increase beginning in late October, with an initial alert on October 27 and seven more alerts before the peak in late November. Laboratory test orders also show an increase in late October with a flatter peak. The first alert in the laboratory test order data is two days after the first alert in the outpatient visit data, on October 29, followed by four more alerts in the next eight days.

In the national capital area, while both data sources show a winter increase in fever syndrome counts, outpatient visits alert on November 17, nearly one month before the first alert in laboratory test order data on December 10. In San Diego, outpatient visits show an initial alert on November 12, followed by a sustained alerting period from November 28 to December 23. Laboratory data show only one alert, a single-day spike on December 18 near the peak of the increase in outpatient visits.

These results suggest that laboratory test order data may be less useful than outpatient visit data for early detection of fever outbreaks, but may be useful for corroborating seasonal increases in fever syndrome.

Summary

Despite the short time frame and lack of documented outbreaks for evaluating syndromic surveillance using laboratory test order data, these results suggest that laboratory test orders may be a useful adjunct to outpatient visit data for detecting and monitoring disease outbreaks. Among the findings;

- Although more respiratory and gastrointestinal outbreaks were detected using outpatient visit data, laboratory test orders detected an outbreak that was not identified in the outpatient visit data.
- Surveillance using a simple EWMA algorithm performed slightly better than the DoD-ESSENCE algorithm with the laboratory test order data.
- Combining the two data sources may yield earlier alerts.
- Case studies indicate that laboratory test orders may be useful for monitoring rash, neurological and fever syndromes.

A further advantage of laboratory test order data is the collection mechanism. A computer record of the laboratory test order is typically produced at the time of order, usually during the outpatient visit. Although these initial records are not currently archived, it would be theoretically possible to develop a system to retrieve these records in real time. Thus alerts might occur earlier in the laboratory data than in the outpatient visit data which are often recorded three or more days after the encounter. Ultimately, this advantage will disappear as the DoD transitions to newer versions of CHCS that will combine clinical and laboratory information in a single record. Despite the limitations of this study, there is sufficient evidence to recommend prospective surveillance using laboratory test data, with further research and evaluation to fine-tune the approach.

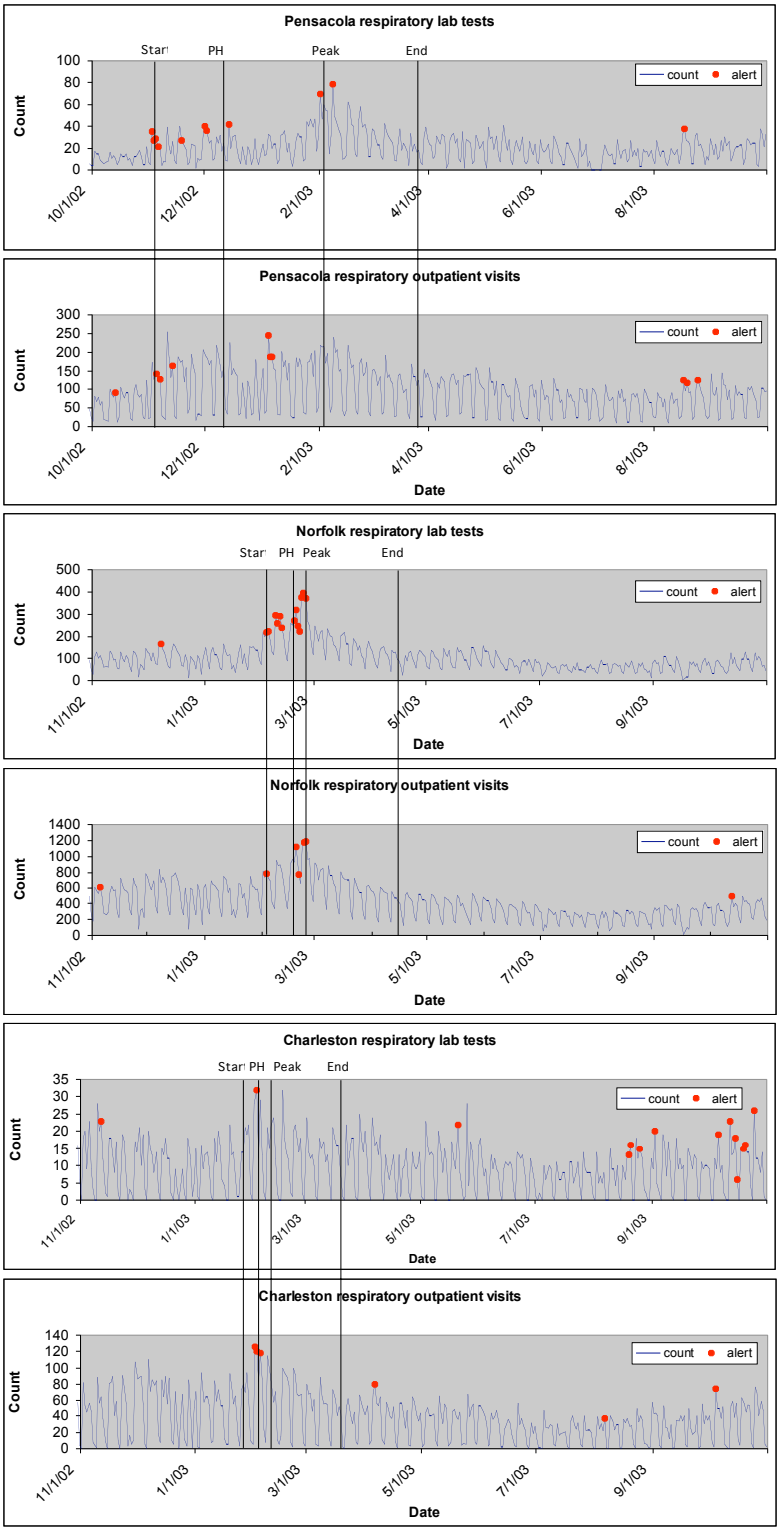


Figure 5.1: Respiratory outbreaks

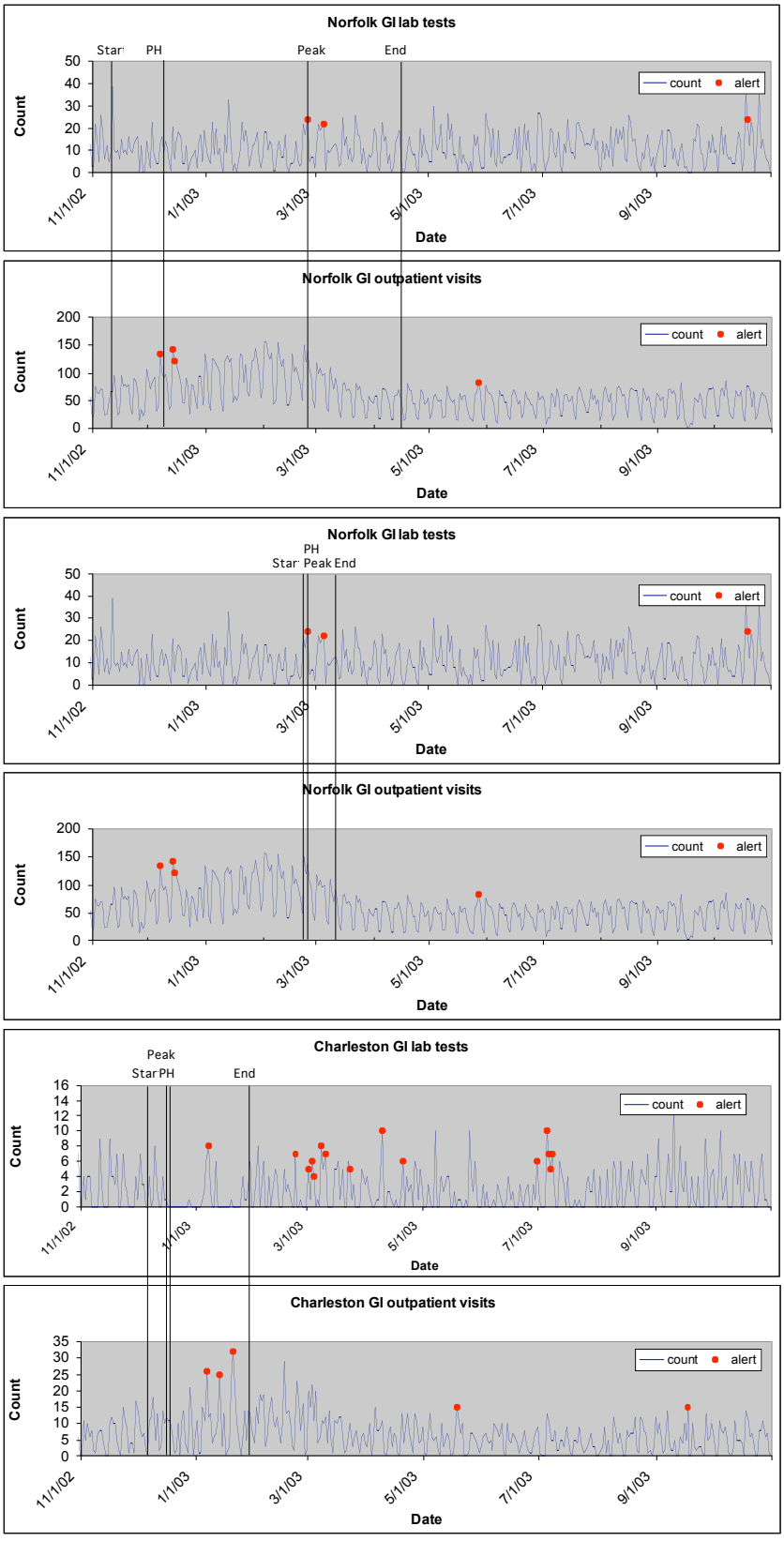


Figure 5.2: Gastrointestinal outbreaks

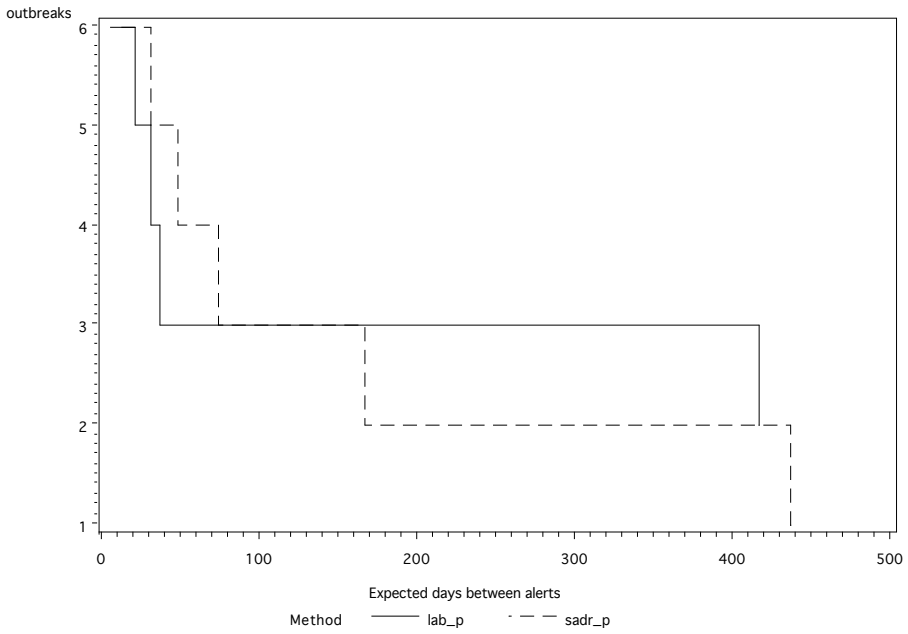


Figure 5.3: Number of outbreaks detected v. background alerting rate, DoD-ESSENCE algorithm

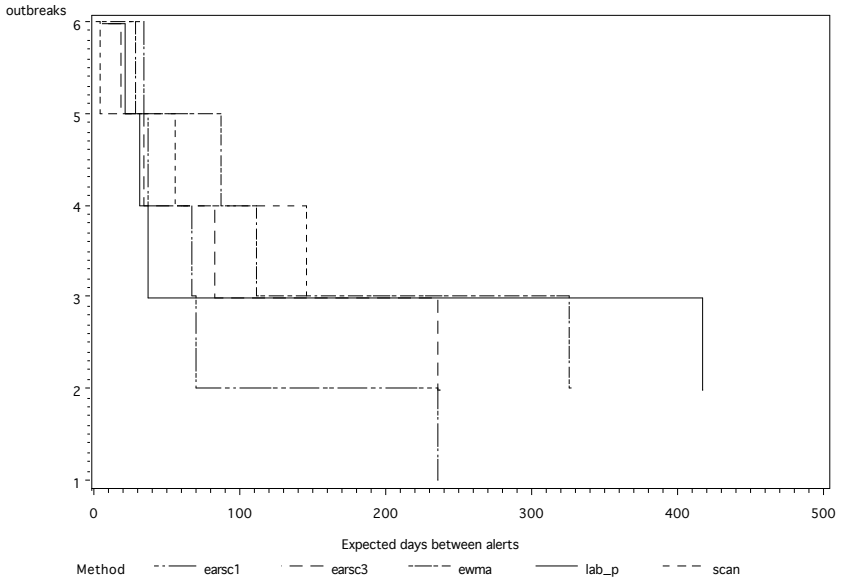
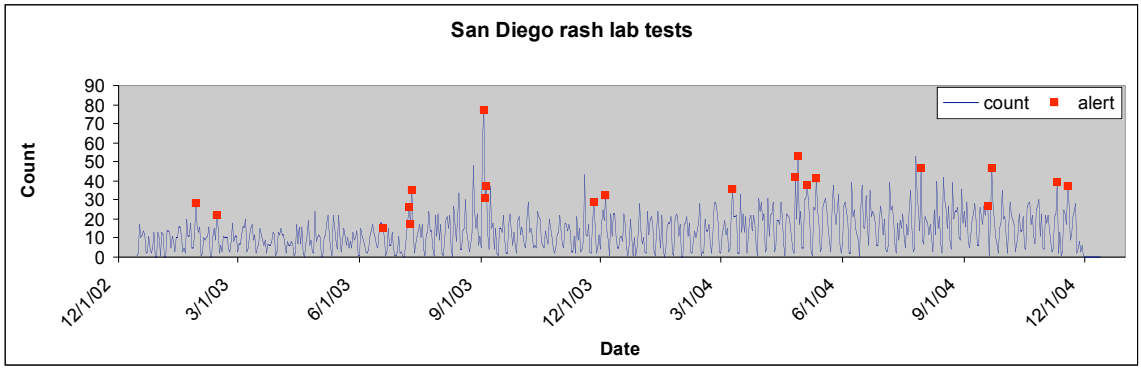
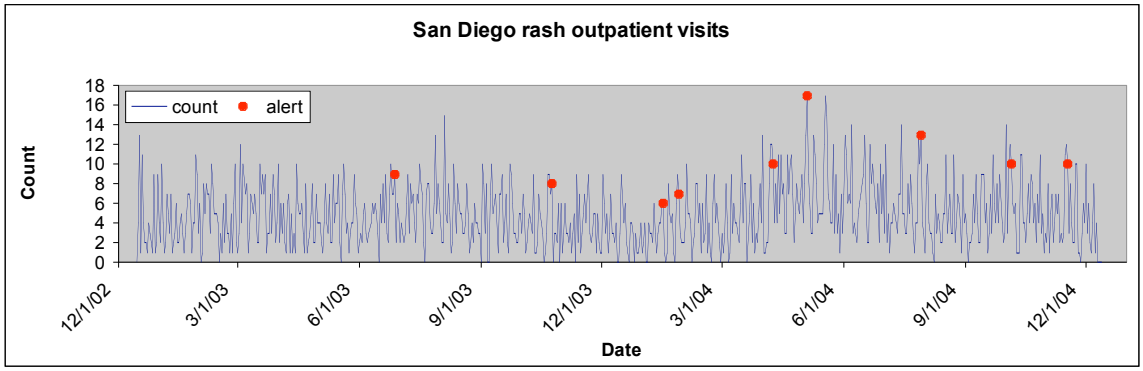
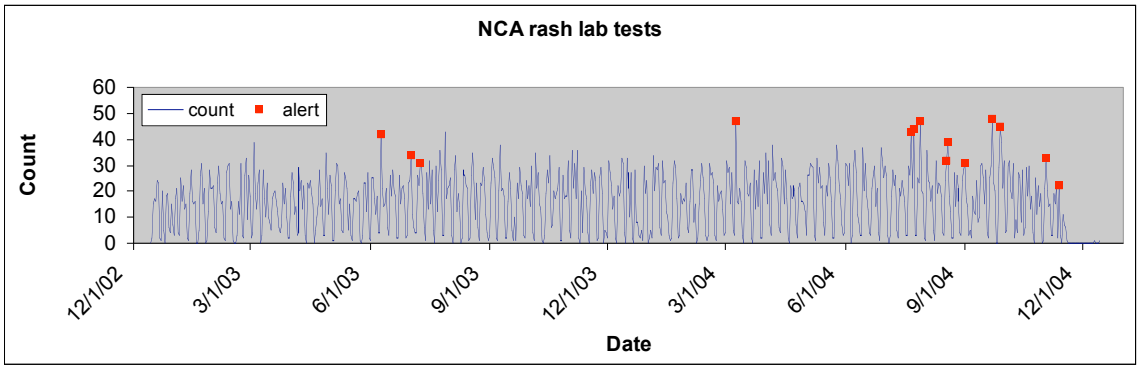


Figure 5.4: Detection v. background alerting rate, laboratory test order data

Figure 5.5. Rash case studies







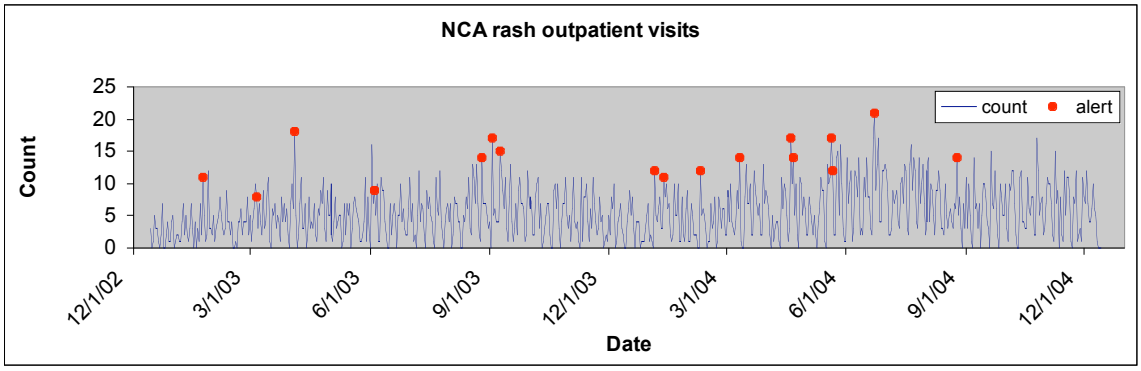
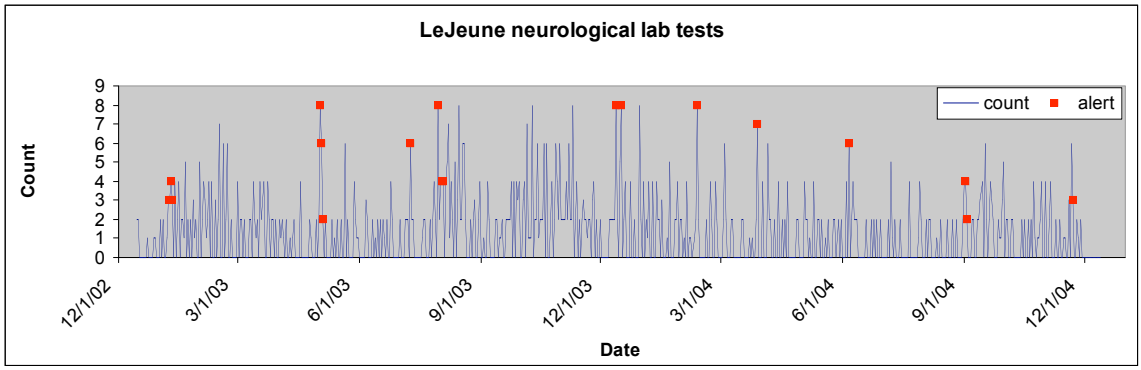
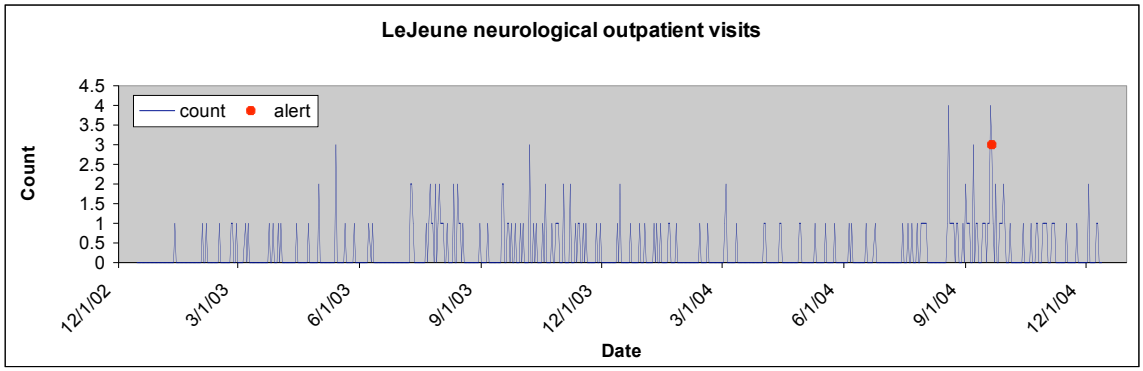
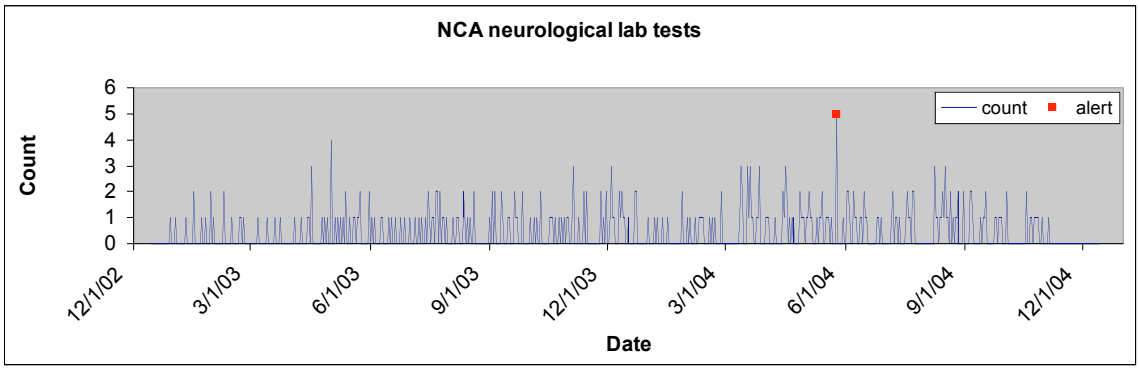
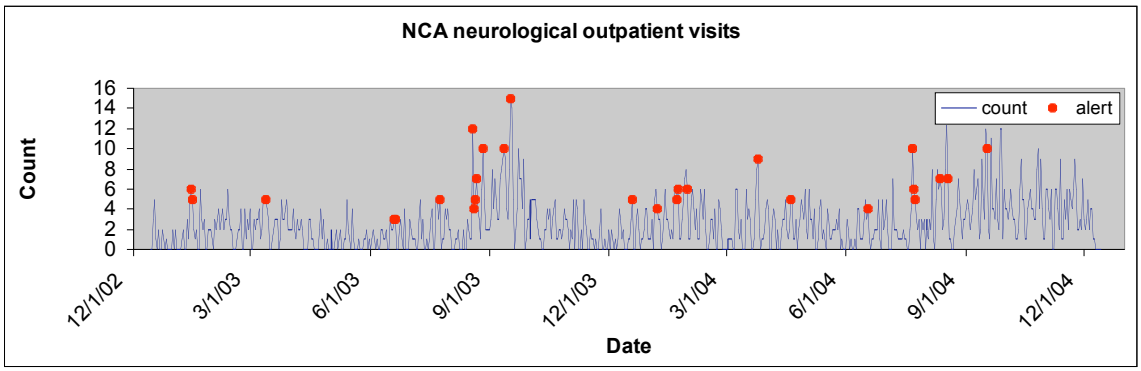


Figure 5.6 Neurological case studies









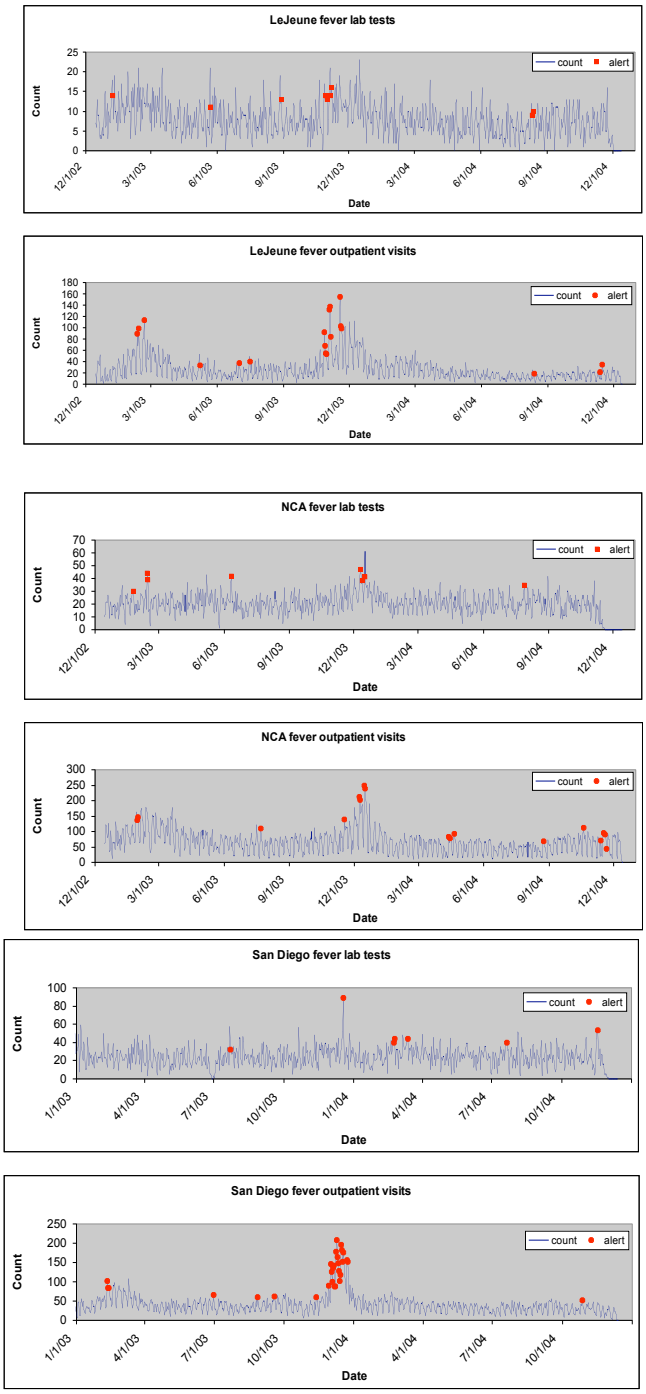


Figure 5.7. Fever case studies

CHAPTER VI: Discussion and conclusion

This study has shown that data on laboratory test orders, currently collected and archived for administrative purposes, may be useful as a supplementary data source for syndromic surveillance. Chapter 6 will summarize and discuss the major findings of the study, address specific findings that may facilitate incorporation of laboratory test order data into ESSENCE, discuss limitations of the study and how to address them in future research, propose next steps for research, and place this work within a broader context of disease surveillance and public health research.

Major results

The goal of the first phase of the study was to develop and validate syndrome definitions comparable to the ICD-9 based syndrome definitions currently used by ESSENCE. The first task was to develop a consistent nomenclature useful for syndromic surveillance. Different laboratories use different nomenclature (e.g. "THR CULT" and "THROAT C" for throat culture) and some laboratory test names are quite general (e.g. "miscellaneous culture", "other culture/sensitivity"). This lack of consistency has been a principal barrier to automated analysis of laboratory test records. It took several months for our panel of three researchers to develop a list of standard test names and map the test names in the database to the standard list. Although there is undoubtedly some misclassification in this scheme, we reviewed the specimen sources associated with each test name and found that they were largely consistent. For example, 99.5 percent of 11,000 cerebrospinal fluid cultures listed a specimen source of cerebrospinal fluid and 99.6 percent of 650,000 throat cultures listed a specimen source of throat or pharynx (the rest were body fluid, swab, or other).

The standard test names are too granular for syndromic surveillance for two reasons. First, syndromic surveillance of 71 test names would be unwieldy and yield too many false alerts. Second, even after the mapping to standard nomenclature, some tests may appear under more than one name. Some labs, for example, listed specific tests for salmonella, shigella and campylobacter under these names while others listed them under the generic "stool culture" category. Surveillance using the test name "Salmonella" would miss a large proportion of tests in which Salmonella is a suspected pathogen. For useful surveillance, the test names should be combined into syndrome groups.

The second task, therefore, was to construct and validate syndrome groups. We had three sources of information against which to validate the syndrome groups: syndromic data based on outpatient ICD-9 diagnostic codes for the same patients, timing and location of known outbreaks, and syndrome groups developed by a CDC panel of physicians and epidemiologists [35]. Although none of the three sources can be considered a true "gold standard", we attempted to construct syndromes that are roughly consistent with all. We assigned a laboratory test to a specific syndrome based on three criteria:

- The test was preferentially ordered during outpatient visits for the syndrome.
- Daily counts of test orders were positively correlated over time with daily counts of outpatient visits for the syndrome in several regions.
- For respiratory and GI syndromes, the number of orders of the laboratory test increased during known outbreaks of the syndrome.

The resulting syndromes were consistent with the syndromes developed by the CDC panel, with a few exceptions discussed in Chapter 4.

Once the syndromes were developed and validated, the second goal of the study was to evaluate the usefulness of laboratory test orders for syndromic surveillance. The primary outcome measures were the number of outbreaks (out of six) that were detected before they would have been recognized by traditional public health surveillance, and the number of days between the start of the outbreak and detection by syndromic surveillance. Three main comparisons were reported: surveillance using laboratory test orders vs. surveillance using outpatient visit diagnoses, using the DoD-ESSENCE algorithm for alerting in both cases; surveillance using the DoD-ESSENCE algorithm vs. surveillance using other commonly-used surveillance algorithms, using the laboratory test order data in all cases, and surveillance using laboratory data combined with outpatient visit diagnoses vs. outpatient visit diagnoses alone, using the DoD-ESSENCE algorithm and simple combination of p-values for combined alerting.

Using an alert rate of one per six weeks, outpatient visit data detected more outbreaks (four of six) than laboratory test order data (two of six). Time to alert was similar for the two data sources: 15 days for outpatient visits data and 17 days for laboratory test order data. These limited findings suggest that laboratory test orders may be useful for syndromic surveillance, but are unlikely to replace outpatient visits as a data source.

One reason laboratory test orders may be less sensitive than outpatient visits for outbreak detection in this study is that during some outbreaks, laboratory tests would be ordered only if identifying the pathogen served an important clinical or public health function. During a gastrointestinal outbreak, for example, clinicians may be unlikely to order a stool culture unless the symptoms are unusual. If this is the case, sensitivity of

laboratory test orders for outbreak detection might be increased during an outbreak of a novel pathogen with unusual symptoms. On the other hand, if laboratory tests are ordered more often for unusual illnesses, this data source may be more specific than outpatient visits for detecting outbreaks outside of seasonal respiratory and gastrointestinal illness. It is not possible to measure specificity directly in this study because for most alerts we cannot determine retrospectively whether an outbreak was present or whether the alert corresponds to a "false positive."

The DoD-ESSENCE algorithm performed fairly well with the laboratory test order data, although there is some evidence that a simple EWMA algorithm would perform even better. One topic for future research would be to evaluate whether adjusting the parameters of the DoD-ESSENCE algorithm would improve its performance relative to EWMA with laboratory data.

When *p*-values from the two data sources were combined, three of six outbreaks were detected, compared with two of six from laboratory test orders alone and four of six from outpatient visit data alone. However, median lag time from the start of the outbreak to the first alert improved markedly, from roughly two weeks for each data source separately to four days for the combined data. Although it would be premature to draw a firm conclusion based on six outbreaks, our results indicate that combining data from multiple data sources may yield a substantial improvement in timeliness of outbreak detection.

Specific findings

In addition to addressing the general questions discussed above, this study was able to shed light on several specific issues:

1. Should surveillance of laboratory tests focus on specific tests, syndrome groups or both?

One way to conduct surveillance of laboratory test orders would be to monitor the frequency of specific tests of interest. This is especially appealing with respect to tests for smallpox, anthrax, and other potential agents of bioterrorism which might get lost in the noise of larger syndromes. The laboratory test orders for these conditions are likely to be much more specific than ICD-9 diagnosis codes based on symptoms and unconfirmed diagnoses. However, there are problems with this approach under the current system. The inconsistent terminology and infrequency of these tests means that we do not know how an anthrax test will be listed when it appears in the data file. The test order name could somehow mention anthrax, but multiple abbreviations are possible. More likely, rare tests would be listed as "miscellaneous culture" or "other", and anthrax would be mentioned only in the results. As an adjunct to daily counts of tests in each syndrome group, it might be useful to scan all records for certain keywords such as "anthrax", using an algorithm that can account for different spellings and abbreviations. This approach should not replace syndromic surveillance, however. Smallpox, for example, might show up in respiratory or fever syndromes under several different test names because of the nonspecific prodrome.

2. *Should the syndromes be based on the test name or specimen source?*

An early proposal for dealing with the lack of consistent nomenclature was to ignore the test names and group tests into syndrome by specimen source. Under this proposal all blood specimens would correspond to the fever syndrome, all stool specimens to the GI syndrome, all throat cultures would correspond to respiratory, and all

skin cultures to rash. While this might yield a reasonable approximation of the syndrome groups, the data suggest that the specimen source field would be less accurate than the test order field. Gastrointestinal and respiratory tests based on specimen source would include tests that are not of interest for syndromic surveillance. For example, 35% of tests with specimen source of "rectum" correspond to GC cultures, group B strep, or herpes tests rather than stool cultures. By comparison, at least 95 percent of tests with the name "stool culture" were obtained from rectal/fecal specimens. There are over 300 tests with a specimen source of "throat" but a test name of GC culture; all tests with the name "throat culture", on the other hand, had specimen source listed as throat specimen or as body fluid/other/swab. The rash syndrome would fail to include ten percent of skin cultures if the definition were based on specimen source. About 90 percent of skin cultures include the word "skin" in the specimen source field, while the rest describe the specific body site, e.g. "scalp", "left leg".

3. Should daily counts be monitored at the MTF or regional level?

At the clinic level, most syndromes have very few laboratory tests. Appendix 2 shows average daily counts of all tests for each MTF included in the study. Counts by syndrome are even lower, with average frequency of test orders less than one per day in nine out of ten clinics for fever, GI, neurological, and rash syndromes. Almost half of clinics have average daily counts less than one for respiratory syndrome, the most prevalent syndrome. Hospitals, on the other hand, make up less than one-quarter of MTFs in this study but account for nearly 60 percent of test orders. It seems likely that monitoring laboratory test orders at every MTF is likely to result in many false alarms based on tiny increases in laboratory test orders. At a facility in which a particular

laboratory test is rarely ordered, even a single order could trigger an alert. A more efficient solution may be to monitor outpatient tests at hospitals. These may represent patients with more severe illness, and the volume of tests is large enough that patterns can emerge. Even better, combining data from a hospital and its affiliated clinics can give a regional picture. One concern is that localized outbreaks may manifest first at local clinics and may be missed by regional surveillance. This may be an acceptable tradeoff for avoiding numerous false alerts, although during periods of heightened concern it may be useful to monitor at the clinic level.

4. How should tests be counted?

The structure of the HL7 files can lead to overcounting of laboratory test orders in two ways. First many duplicate messages are included in the file. This is a technical issue that is easily addressed by searching for and deleting records with duplicate message IDs. However, failure to follow this step can yield misleading results. A more difficult issue is that both "pending" and "final" results are sent for many tests. Pending results account for one-quarter of the records in our data set, and each of these has a corresponding "final" record with a different identifier. Since this study relied on archived data we considered only "final" results. "Pending" results would be a better choice for ongoing surveillance when available because they are available sooner. However, care must be taken to screen out the "final" results corresponding to tests that have already been counted at the "pending" stage. A better approach would be to treat the test order as its own record, separate from the results. This would eliminate the need to consider pending and final records, and could also make the test order information

available at the time of order without the need to wait for certification of results in the laboratory.

Multiple tests per person per day for the same syndrome also can lead to overcounting and false alerts. As discussed in chapter 5, half of the patients for whom a neurological test was ordered had more than one neurological test at the same MTF at the same day. Since neurological tests are rare, two tests for the same person in a single day may trigger an alert. Multiple tests are less of a problem in the other syndromes. Multiple tests are ordered for 29 percent of fever patients, 35 percent of GI patients, 15 percent of rash patients, and 6 percent of respiratory patients. While we did not leave out multiple tests in this study, it would be best to do so in future research.

Limitations

The study has several limitations, mostly related to inadequacies in the data.

1. No gold standard for validation of syndromes.

Two of the three validation criteria in Chapter 4 were based on outpatient visit syndromes. Laboratory test orders are considered to be associated with a syndrome if they are preferentially ordered during outpatient visits for that syndrome, and if daily counts of laboratory tests orders are correlated over time with daily counts of outpatient visits for a particular syndrome. However, there is no guarantee that syndromes based on ICD-9 diagnosis codes reflect actual illness with a particular syndrome. Use of ICD-9 codes can be highly idiosyncratic. The gold standard for assigning a patient to a particular syndrome is physician chart review. A previous study by Foster et al. [13] showed that across three syndromes and several emergency departments, classification of outpatient visits based on ICD-9 diagnosis codes agreed closely with physician chart

review. Most patients diagnosed with a syndrome based on chart review also were assigned to that syndrome based on ICD-9 codes (sensitivity, 67-95 percent), and few patients were assigned to a syndrome based on their ICD-9 diagnosis codes without corresponding symptoms noted in their chart (specificity, 92-97 percent). So despite the impossibility of using chart reviews as a gold standard for this study, using ICD-9-based syndromes as a surrogate seems reasonable.

2. Too few outbreaks.

In this study, four confirmed outbreaks were used to validate the syndrome groupings, and six outbreaks were used to evaluate sensitivity and timeliness of outbreak detection. All of these outbreaks corresponded to respiratory or gastrointestinal syndromes, so we could not evaluate the remaining syndromes with respect to confirmed outbreaks. Many more outbreaks would be needed to obtain reliable estimates of sensitivity and timeliness even for respiratory and gastrointestinal syndromes.

It was not possible to identify more outbreaks because the data available for the study correspond to a two-year period that ended two years before the analysis. With current data, it might have been possible to identify increases in outpatient visits or laboratory test orders, and then contact MTFs to determine whether the increases represented actual outbreaks or not. But contacting MTFs about potential outbreaks that occurred more than two years ago did not seem like a fruitful strategy.

One way to overcome this limitation would be to use simulated outbreaks. Using this approach, extra laboratory test orders would be injected into either actual data or simulated data representing the background rate of laboratory test orders in the absence of an outbreak. The distribution of the injected data would be based on models of disease

exposure, incubation periods, and expected health care utilization (e.g. Coberley et al. [71]). The missing piece of the simulation model for this study is health care utilization. Modeling the proportion of ill persons who would have an outpatient visit, and the proportion of those with an outpatient visit who would get a particular laboratory test, is beyond the scope of this study.

As part of the data analysis presented in Chapter 4, we calculated the proportion of outpatient visits in each ICD-9 based syndrome that have a corresponding laboratory test for that syndrome (data not shown). This could be an important part of building a model for simulating disease outbreaks in laboratory test order data. Physicians typically order one fever test per 102 fever visits, one GI test per 63 GI visits, one neurological test per 27 neurological visits, one rash test per 450 rash visits, and one respiratory test per 18 respiratory visits. However, we still do not know whether the proportions would change during an outbreak. It seems likely that, once an outbreak diagnosis is established, test ordering will decrease even if the outbreak is ongoing, because new cases wil be assumed to be part of the outbreak. The Charleston GI outbreak described in chapter 5 showed this pattern, with tests "bottoming out" for several days after the public health recognition date. Future research could investigate whether this is a consistent pattern.

3. Misclassification of tests.

Tests may be misclassified on two levels. First, the test name on the laboratory test record may be assigned to the wrong standardized test name. For example, while the vast majority of laboratory tests assigned to the "CSF CULTURE" standardized test name listed cerebrospinal fluid as the specimen source, there were ten "CSF CULTURE" tests that listed the specimen source as "blood". It is impossible to determine whether the

test name or the specimen source is in error, so for some of these cases, they may be incorrectly classified as CSF cultures. Although this type of mismatch is relatively rare, it illustrates that the data set does not always provide sufficient or consistent information to assign tests to the appropriate category.

Second, tests may be assigned to the wrong syndrome group. For example, over 3,000 tests are listed as "miscellaneous culture" or similar on the test records. These tests are only assigned to a syndrome if the specimen source falls unambiguously into one of the syndromes (blood for fever, stool for GI, CSF for neurological, throat/pharynx for respiratory.) The 70 cultures with specimen source of "leg" or "scalp" are probably skin or wound cultures that could be assigned to the rash syndrome if more information were available.

A potential consequence of misclassification is that it could attenuate the signals seen in the data relative to the noise. Small to moderate increases in laboratory tests for a particular syndrome will appear even smaller if many of the laboratory tests associated with the increase are not included in the appropriate syndrome. Standardizing laboratory test order nomenclature, for both test names and specimen sources, can go a long way towards fixing this problem. In the mean time, it appears that even with the potential misclassification, laboratory test order data are still useful for detecting outbreaks.

4. Data include only microbiology laboratory tests.

Test orders are broadly categorized as microbiology, chemistry, or radiology in the HL-7 records. This study evaluated only microbiology data because the total volume of test records was so large that processing the archived data would have been prohibitive, and microbiology tests are expected to be most specific for infectious

diseases. However, particular chemistry tests may be useful for monitoring infectious disease syndromes. One of the most promising candidates is rapid influenza tests. Asha Riegododios at the Navy Environmental Health Center has plotted daily counts of these tests for one MTF and they show a stronger seasonal pattern than is observed in throat cultures (personal correspondence). Obtaining data on additional tests should be a high priority for future research.

5. Incomplete data.

The time frame for this study occurred before many of the MTFs began submitting laboratory test records to the HL7 archive. Air Force facilities in particular were less likely to participate before the fall of 2004. Thus the sample is heavily weighted towards Army and Navy MTFs. The assignment of laboratory test names to standardized categories will have to be re-evaluated in current data to ensure that laboratory test names used in the MTFs that came online after the study ended are assigned to the appropriate categories. This problem can be resolved over time as MTFs become more familiar with the system and adopt a standardized nomenclature.

Future research

Several topics for future research were mentioned above: continuing the study with more outbreaks and current data to determine whether the findings hold up, developing a model of test ordering behavior and using the model to simulate outbreaks, adjusting the parameters of the DoD-ESSENCE algorithm, and incorporating data on chemistry tests. Several additional research questions may also be of interest

1. Is immediate electronic capture of test orders feasible?

This study suggests that if laboratory data are to improve timeliness of outbreak detection, much of that improvement must come from earlier electronic capture of laboratory test order records. Laboratory tests are generally ordered during an outpatient visit, so they are unlikely to show an earlier signal than outpatient visits otherwise. The fact that laboratory tests are typically ordered electronically indicates that it should be feasible to capture the electronic record at the time of order. It would be worthwhile to determine the modifications to the computer system that would be required to implement immediate capture of laboratory test orders.

2. Are daily counts the best measure of laboratory test orders?

The results of this study suggest that joint surveillance of both outpatient visits and laboratory test orders can improve the timeliness of outbreak detection. The method used was a simple combination of p-values, and a more sophisticated method for combining data might yield better results. One assumption of many methods for multivariate surveillance is that the data streams are independent. Since nearly all laboratory tests are ordered during an outpatient visit, this assumption must be false. One suggestion for addressing this issue is to monitor the ratio of laboratory tests to outpatient visits rather than daily counts of outpatient visits. This suggestion is intuitively appealing because it may be that physicians order tests for a higher proportion of their patients during an outbreak of an unknown illness. A future research project could evaluate which approach leads to better outbreak detection.

3. Does linking laboratory tests with corresponding outpatient visits yield better surveillance?

As described above, it may be useful to monitor the ratio of laboratory tests to outpatient visits. This could be done by calculating daily counts separately from each data source and taking a simple ratio. An extension of this research question is whether it would be even better to monitor the proportion of tests for a particular syndrome in which a laboratory test for that syndrome is ordered. Similarly, it might be useful to monitor daily counts of patients with both an outpatient visit and a laboratory test order for the same syndrome. This would require linking laboratory tests to the outpatient visits during which they were ordered. Then, for example, throat cultures that were ordered without a corresponding respiratory diagnosis would not be counted. The analysis in Chapter 4 demonstrates that this linking is feasible, if computationally intensive. It would be worthwhile to evaluate whether linking records would yield a gain in outbreak detection that outweighs the additional complexity.

4. Do specific population subgroups provide earlier indication of outbreaks?

Demographic subgroups, specifically children, have been shown to be sentinel populations for influenza [72]. An unpublished analysis of outpatient visit records used in DoD-ESSENCE indicated that when outpatient visits for respiratory syndrome are analyzed separately by age group, seasonal increases do not occur earlier in children than in adults. Because of the inconsistent findings across data sets, it would be worthwhile to evaluate whether outbreaks alert earlier in the laboratory test data for specific age groups.

5. Can automated surveillance be performed on laboratory test results?

Surveillance of laboratory test results would not be particularly useful for early detection of outbreaks because of the time delay between onset of symptoms and certification of results. However, automated surveillance of laboratory test results would

be tremendously useful in other ways. During an outbreak, automated surveillance could identify cases who could then be contacted as part of an epidemiological investigation. Identifying the pathogen responsible for the outbreak would be facilitated by having an electronic record of all test results during the time period. Reportable diseases could be monitored automatically using existing records, potentially eliminating the need for a separate reporting system and reducing the reporting burden on physicians and laboratories. Research of this type is ongoing at the Navy Environmental Health Center, and much more is needed.

Public health significance

This study makes several novel contributions to public health. This is the first systematic evaluation of DoD laboratory test data for general public health surveillance. While Riegododios et al have used DoD laboratory data for surveillance of specific illnesses [31-34], this study complements that research by expanding the focus to syndromic surveillance. The CDC has incorporated laboratory test data from LabCorp, a nationwide laboratory system for syndromic surveillance that tests more than 340,000 specimens daily (Ma et al., 2005). This is the only other study of a nationwide laboratory data source for syndromic surveillance, the first attempt to validate such a source against outpatient visit data, and the first to evaluate outbreak detection using laboratory data.

One stated goal of syndromic surveillance is "to enable earlier detection of epidemics and a more timely public health response, hours or days before disease clusters are recognized clinically, or before specific diagnoses are made and reported to public health authorities" [1]. Early syndromic surveillance systems were developed specifically to detect bioterrorist attacks such as anthrax and smallpox. Since then, public

health attention has become more focused on emerging infectious diseases, including SARS and pandemic influenza. Regardless of the source of the threat, early detection of outbreaks can lead to early intervention and mitigate the costs of the outbreak. This study is the first to show that incorporating laboratory test orders into an existing surveillance system can improve the timeliness of outbreak detection.

While early detection is still a primary goal, research in syndromic surveillance has expanded to include ongoing situational awareness. The CDC, for example, now refers to its BioSense program as a system for "early event detection and situational awareness." Once an outbreak is detected, syndromic surveillance can monitor whether the number of cases is increasing or decreasing, describe the demographic and geographic distribution of cases, and provide other useful information without adding to the workload of clinicians. This evaluation of laboratory test data is an important first step towards being able to monitor not just syndromes, but laboratory-confirmed diagnoses, during an outbreak.

Electronic records have the potential to revolutionize public health research. Because the data are collected anyway for clinical and billing purposes, there is no additional burden for clinical staff to collect data specifically for research. Rare illness may be studied because the huge quantity of administrative records makes it possible to identify many people with a specific illness, even if a specific provider may only see a handful of such patients. Linkage of hospital, clinic, pharmacy and laboratory records makes it possible to gain a thorough clinical picture and track patients through the system over time. Laboratory data may useful not only for syndromic surveillance, but as part of an overall trend towards leveraging administrative data for public health research. While

there is much work left to be done, this study shows that it is feasible to obtain useful public health information from DoD laboratory test data, and to link this information to other claims for the same patients.

In summary, this study demonstrates that laboratory test order data can improve the performance of the DoD-ESSENCE syndromic surveillance system. Laboratory test data will undoubtedly prove useful for many other types of public health research. Surveillance and research would be greatly facilitated if the DoD would adopt a standard terminology across the entire military health system.

Appendix 1: CDC laboratory syndrome definitions

syndrome_name	syndrome_definition	Laboratory tests
Gastrointestinal	ACUTE infection of the upper and/ or lower gastrointestinal (GI) tract; SPECIFIC diagnosis of acute GI distress such as Salmonella gastroenteritis; ACUTE non-specific symptoms of GI distress such as nausea, vomiting, or diarrhea; EXCLUDES any chronic conditions such as inflammatory bowel syndrome.	Helicobacter pylori Culture H PYLORI, IGM, IGG, IGA AB H. pylori IgG, Abs H. pylori Stool Antigen Helicobacter pylori, IgA Helicobacter pylori, IgM Ab C difficile Toxin A C difficile, Toxin B/Cytotoxin Clostridium difficile Culture Campylobacter Culture Enterohemorrhagic E coli Cult Adenovirus (40/41)/Rotavirus Adenovirus (40/41), Direct EIA Norovirus, RT-PCR Rotavirus Detection by EIA Cryptosporidium Smear, Stool Amebiasis Antibodies Cyclospora Smear, Stool Giardia lamblia, Direct, EIA Giardia, EIA; Ova/Parasites Stool Culture Stool Culture, Yersinia Only Stool Culture, Vibrio Only White Blood Cells (WBC), Stool Occult Blood, Stool Ova/Parasites Exam, Routine Fecal Reducing Substances
Respiratory	ACUTE infection of the upper and/ or lower respiratory tract (from the oropharynx to the lungs, includes otitis media); SPECIFIC diagnosis of acute respiratory tract infection (RTI) such as pneumonia due to parainfluenza virus; ACUTE non-specific diagnosis of RTI such as sinusitis, pharyngitis, laryngitis ACUTE non-specific symptoms of RTI such as cough, stridor, shortness of breath, throat pain; EXCLUDES chronic conditions such as chronic bronchitis, asthma without acute exacerbation, chronic sinusitis, allergic conditions (Note: INCLUDE acute exacerbation of chronic illnesses.)	AFB Cult/Smear, Broth, Suscep AFB Culture and Smear, Broth Organism ID, Mycobacteria M tuberculosis Detection, PCR M tuberculosis, PCR/Culture Mycoplasma pneumoniae Culture Mycoplasma Pneumoniae, PCR Mycoplasma pneu. IgG/IgM Abs Mycoplasma pneumoniae, IgG Ab

syndrome_name	syndrome_definition	Laboratory tests
		Mycoplasma pneumoniae, IgM Ab Adenovirus Group Ab, Qn Adenovirus Detection by PCR Virus, Adenovirus by DFA B pertussis Smear, DFA B pertussis IgA Ab, Quant B pertussis IgG/M/A Ab, Quant B pertussis, Nasophar Culture Bordetella Para&Pertussis PCR B pertussis IgG Ab, Quant B pertussis IgG/IgM Ab, Quant B pertussis IgM Ab, Quant Beta-Hemolytic Strep, A Only Streptococcus pneumoniae Ag Beta Strep (Group B) Antigen Chlamydia psittaci Culture Chlamydia Pneumoniae PCR Haemophilus influenzae B Ag Haemophilus influenzae B IgG Influenza A Only by Direct EIA Viral Culture,Rapid,Influenza Influenza A/B Ab, Quant Influenza A & B, Immunoassay Parainfluenza Virus Antibody Legionella Species Culture Legionella pneumophila Ur Ag Legionella pneumophila by DFA Legionella pneumophila/Culture RSV Ab, Quant Virus, RSV by DFA RSV by EIA Upper Respiratory Culture Lower Respiratory Culture Viral Culture,Rapid,Respirator

syndrome_name	syndrome_definition	Laboratory tests
		Brucella abortus IgG, EIA Brucella abortus IgM, EIA Diphtheria Antitoxoid Ab Q Fever Antibodies, IgG RESPIRATORY INFECTION PROF A RESPIRATORY INFECTION PROF B Respiratory Infection Prof D Fungal Antibodies, Quant Histoplasma Abs, Qn, DID
Fever	ACUTE potentially febrile illness of origin not specified; INCLUDES fever and septicemia not otherwise specified; INCLUDES unspecified viral illness even though unknown if fever is present; EXCLUDE entry in this syndrome category if more specific diagnostic code is present allowing same patient visit to be categorized as respiratory, neurological or gastrointestinal illness syndrome.	Aerobic Bacterial Culture Anaerobic Culture Anaerobic and Aerobic Culture Blood Culture, Routine Viral Culture, General Anaerobic/Aerobic/Gram's Stain Febrile Agglutinin Panel Malarial Smear Ehrlichia Ab Panel Human Gran. Ehrlichiosis (IgG) Human Monocytic Ehrlich-PCR E. chaffeenis-HME (Monocytic) Ehrlichia Detection by PCR Human Granulocytic Ehrlich-HGE Gram's Stain Aerobe ID & Suscept Anaerobe Identification Only MRSA Culture Only MRSA Culture/Susceptibility Vancomycin-Resist Enterococcus MIC/Min Bactericidal Conc
Neurological	ACUTE neurological infection of the central nervous system (CNS); SPECIFIC diagnosis of acute CNS infection such as pneumoccocal meningitis, viral encephailitis; ACUTE non-specific diagnosis of CNS infection such as meningitis not otherwise specified (NOS), encephailitis NOS, encephalopathy NOS ACUTE non-specific symptoms of CNS infection such as meningismus, delerium; EXCLUDES any chronic, hereditary or degenerative conditions of the CNS such as obstructive hydrocephalus, Parkinson’s, Alzheimer’s.	Glucose, Cerebrospinal Fluid Protein, Total, CSF Bacterial Antigens Cell Count, CSF Calif Encephalitis Ab, IgG Calif Encephalitis Ab, IgM India Ink Preparation Cryptococcus Antibodies, Quant Cryptococcus Antigen, CSF Cryptococcus Antigen, Serum East Eq Encephalitis Ab, IgG

syndrome_name	syndrome_definition	Laboratory tests
		East Eq Encephalitis Ab, IgM St Louis Enceph V Ab, IgG St Louis Enceph V Ab, IgM Western Equine Enceph Ab, IgG Western Equine Enceph Ab, IgM West Nile Virus Antibody,Serum West Nile Virus, RT-PCR West Nile Virus Antibody, CSF Arboviral Encephalitis Ab, IgM Arboviral Encephalitis Ab, IgG JC/BK Virus DNA PCR Enterovirus RT-PCR Lyme Ab/Total Immunoglobulins LYME/SYPHILIS AB DIFF PROFILE Lyme Ab, Total/IgM Responses Lyme Ab/Western Blot Reflex Lyme Disease(B.Burgdorferi)PCR Lyme PCR, Borrelia burgdorferi Lyme, IgM, Early Test/Reflex Lyme, Total Ab Test/Reflex Lyme, Western Blot, Serum Lyme, Western Blot, Syn Fluid
Botulism-like	ACUTE condition that may represent exposure to botulinum toxin; ACUTE paralytic conditions consistent with botulism: cranial nerve VI (lateral rectus) palsy, ptosis, dilated pupils, decreased gag reflex, media rectus palsy. ACUTE descending motor paralysis (including muscles of respiration); ACUTE symptoms consistent with botulism: diplopia, dry mouth, dysphagia, difficulty focusing to a near point.	None
Hemorrhagic Illness	SPECIFIC diagnosis of any virus that causes viral hemorrhagic fever (VHF): yellow fever, dengue, Rift Valley fever, Crimean-Congo HF, Kyasanur Forest disease, Omsk HF, Hantaan, Junin, Machupo, Lassa, Marburg, Ebola; ACUTE condition with multiple organ involvement that may be consistent with	None

syndrome_name	syndrome_definition	Laboratory tests
	exposure to any virus that causes VHF; ACUTE blood abnormalities consistent with VHF: leukopenia, neutropenia, thrombocytopenia, decreased clotting factors, albuminuria.	
Lymphadenitis	ACUTE regional lymph node swelling and/ or infection (painful bubo- particularly in groin, axilla or neck)	Cytomegalovirus (CMV) Culture Virus, Cytomegalovirus by DFA Cytomegalovirus Quant. PCR Cytomegalovirus (CMV) Ab, IgM CMV PCR Southern Blot CMV DNA Probe, Paraffin CMV PCR Detect.,Amniotic Fluid Viral Culture, Rapid, CMV Mono Qual W/Rflx Qn Mononucleosis Test, Qual EBV Ab VCA, IgG EBV Early Antigen Ab Prof, Qn EBV Early Antigen Ab, IgG EBV Ab VCA, IgM Epstein-Barr Virus Real Time Epstein-Barr DNA PCR Real Time Epstein-Barr Virus, DNA Probe Mumps Antibodies, IgG Tularemia Agglutinins Toxoplasma gondii Ab, IgG, Qn Toxoplasma Gondii PCR

syndrome_name	syndrome_definition	Laboratory tests
Localized Cutaneous Lesion / Rash	SPECIFIC diagnosis of localized cutaneous lesion/ ulcer consistent with cutaneous anthrax or tularemia; ACUTE localized edema and/ or cutaneous lesion/ vesicle, ulcer, eschar that may be consistent with cutaneous anthrax or tularemia; INCLUDES insect bites; EXCLUDES any lesion disseminated over the body or generalized rash; EXCLUDES diabetic ulcer and ulcer associated with peripheral vascular disease. ACUTE condition that may present as consistent with smallpox (macules, papules, vesicles predominantly of face/arms/legs); SPECIFIC diagnosis of acute rash such as chicken pox in person > XX years of age (base age cut-off on data interpretation) or smallpox; ACUTE non-specific diagnosis of rash compatible with infectious disease, such as viral exanthem; EXCLUDES allergic or inflammatory skin conditions such as contact or seborrheaic dermatitis, rosacea; EXCLUDES rash NOS, rash due to poison ivy, sunburn, and eczema.	Rocky Mtn Spotted Fev, IgG, Qn Rocky Mtn Spotted Fever, IgM Rubella Antibodies, IgM Rubella Antibodies, IgG Human Papillomavirus, Biopsy Human Papillomavirus, PCR Viral Culture,Rapid,Varicella Virus, Varicella Zoster by DFA Varicella-Zoster Ab, IgM Varicella-Zoster V Ab, IgG VZV Real Time PCR Parvovirus B19 PCR Amn. Fl Det Parvovirus B19 PCR Detection RASH PROFILE B Rash Profile A Measles/Mumps/Rubella Immunity Rubeola Antibodies, IgG HHV-6, IgG Antibodies, Quant Viral Culture,Rapid,Lesion Virus, HSV by DFA HSV 1/2 PCR HSV Culture and Typing HSV I/II, IgG/Rfx Type II IgG HSV Type 2-Specific Ab, IgG HSV, IgM I/II Combination Herpes Simplex Virus, DNA HSV Culture Without Typing Herpes Simplex Virus I/II, IgG Dermatophyte Only, Culture
Specific Infection	ACUTE infection of known cause not covered in other syndrome groups, usually has more generalized symptoms (i.e., not just respiratory or gastrointestinal); INCLUDES septicemia from known bacteria; INCLUDES other febrile illnesses such as scarlet fever.	Organism ID, Bacteria Organism Identification, Yeast Genital Culture, Routine Urine Culture, Comprehensive Reference Bacterial Culture ID Susceptibility, Aer & Anaerob Parasite Identification Fungus (Mycology) Culture Fungus Stain

syndrome_name	syndrome_definition	Laboratory tests
		Fungus Culture With Stain Candida Antibodies, Qual Anti-DNase B Strep Antibodies Tetanus/Diphtheria Ab Chlamydia Antibodies, IgG Chlamydia trach.Swab/Urine,PCR Chlamydia trachomatis Ab, IgM Chlamydia trachomatis Culture Echinococcus Antibody Hep A Ab, IgM Hep A Ab, Total Hep B Core Ab, IgM Hep B Core Ab, Tot Hep B Surface Ab Hep B Surface Ag Hep Be Ab Hep Be Ag Hep C Virus Ab HAV/HBV (Profile VII) HBV Core Ab, IgG/IgM Diff HBV/HCV (Profile VIII) HCV QuantaSure Plus (Serial) HCV QuantaSure Plus(Non-Graph) HCV RNA by PCR, Qn Rfx Geno HCV RNA, PCR, Qualitative Hepatitis A (Prof V) Hepatitis B Virus (Profile VI) Hepatitis C Virus Genotyping Hepatitis Follow-Up (Prof II) Hepatitis Panel (4) Hepatitis Pt Mgmnt (Prof III) Hepatitis, Diagnostic (Prof I) NGI HBV SuperQuant NGI HBV UltraQual NGI HCV QuantaSure NGI HCV SuperQuant NGI HCV UltraQual HAV/HBV Immune Status (Pro IV) HBV DNA, Qualitative PCR HBV Follow-Up (Profile XII) HBV Prevaccination (Profile X) HBV Vaccine Follow-Up (Pro XI) HCV RNA Det Ql Rfx Gen

syndrome_name	syndrome_definition	Laboratory tests
		HCV RNA by PCR, Qn Rfx Geno HCV RNA, PCR, Ql (Quant Rflx) Hepatitis B, Prenatal (Prof X Strep pneumo IgG Ab (6 Sero) Strep pneumo IgG Ab (7 Sero.) Strep. pneumo.IgG Ab (4 Sero.) Strep.pneumo.IgG Ab (14 Sero) Prenat Infect Dis Ab, IgG, Qn Prenat Infect Dis Ab, IgM, Qn HTLV-I/II Antibodies, Qual Ureaplasma/Mycoplasma hominis
Severe Illness or Death potentially due to infectious disease	ACUTE onset of shock or coma from potentially infectious causes; EXCLUDES shock from trauma; INCLUDES SUDDEN death, death in emergency room, intrauterine deaths, fetal death, spontaneous abortion, and still births; EXCLUDES induced fetal abortions, deaths of unknown cause, and unattended deaths.	None

Appendix 2: MTFs with complete data

Facility Name	DMIS ID	Branch of service	Facility Type	US Flag?	Avg. daily tests
11TH MED GRP-BOLLING	0413	F	CLINIC	Y	16
14th MED GRP-COLUMBUS	0074	F	CLINIC	Y	3
15th MED GRP-HICKAM	0287	F	CLINIC	Y	10
16th MED GRP-HURLBURT FIELD	7139	F	CLINIC	Y	14
18th MED GRP-KADENA AB	0804	F	CLINIC	N	18
1st MED GRP-LANGLEY	0120	F	HOSP	Y	74
20th MED GRP-SHAW	0101	F	HOSP	Y	16
27th MED GRP-CANNON	0085	F	CLINIC	Y	15
30th MED GRP-VANDENBERG	0018	F	CLINIC	Y	11
319th MED GRP-GRAND FORKS	0093	F	CLINIC	Y	7
31st MED GRP-AVIANO	0808	F	HOSP	N	12
325th MED GRP-TYNDALL	0043	F	CLINIC	Y	14
341st MED GRP-MALMSTROM	0077	F	CLINIC	Y	7
354th MED GRP-EIELSON	0203	F	CLINIC	Y	12
366th MED GRP-MOUNTAIN HOME	0053	F	HOSP	Y	14
374th MED GRP-YOKOTA AB	0640	F	HOSP	N	25
3rd MED GRP-ELMENDORF	0006	F	HOSP	Y	40
401 EABG/SG-TUZLA AB	6704	F	ADMIN	N	1
422 ABS MED FLT-CROUGHTON	0653	F	CLINIC	N	2
423RD ABS OL-A-RAF UPWOOD	0814	F	CLINIC	N	2
437th MED GRP-CHARLESTON	0356	F	CLINIC	Y	18
469th MED FLT-RHEIN MAIN	0800	F	CLINIC	N	4
470 MED FLT-GEILENKIRCHEN	0799	F	CLINIC	N	2
48th MED GRP-LAKENHEATH	0633	F	HOSP	N	35
4th MED GRP-SEYMOUR JOHNSON	0090	F	CLINIC	Y	17
51st MED GRP-OSAN AB	0638	F	HOSP	N	10
52nd MED GROUP-SPANGDAHLEM	0805	F	HOSP	N	19
56th MED GRP-LUKE	0009	F	HOSP	Y	48
5th MED GRP-MINOT	0094	F	CLINIC	Y	10
601st MED SQUAD-SEMBACH	0801	F	INACT	N	22
60th MED GRP-TRAVIS	0014	F	HOSP	Y	79
61st MED SQUAD-LOS ANGELES	0248	F	CLINIC	Y	6
66th MED GRP-HANSCOM	0310	F	CLINIC	Y	11
6th MED GRP-MACDILL	0045	F	HOSP	Y	76
7020th ABG CLINIC-FAIRFORD	0815	F	CLINIC	N	0
74th MED GRP-WRIGHT-PATTERSON	0095	F	HOSP	Y	115
75th MED GRP-HILL	0119	F	CLINIC	Y	37
7th MED GRP-DYESS	0112	F	CLINIC	Y	14
82nd MED GRP-SHEPPARD	0113	F	HOSP	Y	35
89th MED GRP-ANDREWS	0066	F	HOSP	Y	99

Facility Name	DMIS ID	Branch of service	Facility Type	US Flag?	Avg. daily tests
8th MED GRP-KUNSAN AB	0637	F	CLINIC	N	2
90th MED GRP-F.E. WARREN	0129	F	CLINIC	Y	19
96th MED GRP-EGLIN	0042	F	HOSP	Y	65
9th MED GRP-BEALE	0015	F	CLINIC	Y	14
AHC BAUMHOLDER	1007	A	INACT	N	9
AHC BRUSSELS	8977	A	CLINIC	N	0
AHC BUTZBACH	8996	A	CLINIC	N	2
AHC COLEMAN	7152	A	CLINIC	N	1
AHC DARMSTADT	8998	A	CLINIC	N	5
AHC DEXHEIM	8992	A	CLINIC	N	1
AHC FRIEDBERG	1135	A	CLINIC	N	1
AHC FT. STORY	0464	A	CLINIC	Y	1
AHC GIEBELSTADT	1235	A	CLINIC	N	1
AHC GRAFENWOEHR	1016	A	CLINIC	N	1
AHC HANAU	8995	A	CLINIC	N	7
AHC HOHENFELS	1019	A	CLINIC	N	2
AHC ILLESHEIM	1014	A	CLINIC	N	1
AHC KAISERSLAUTERN	1128	A	CLINIC	N	3
AHC KATTERBACH	1015	A	CLINIC	N	2
AHC KELLY-STUTTGART	1233	A	INACT	N	5
AHC KITZINGEN	1127	A	CLINIC	N	2
AHC LIVORNO	1154	A	CLINIC	N	1
AHC MANNHEIM	1003	A	CLINIC	N	9
AHC MCAFEE-WHITE SANDS MSL RAN	0327	A	CLINIC	Y	1
AHC SCHWEINFURT	1124	A	CLINIC	N	4
AHC SHAPE	0614	A	CLINIC	N	4
AHC VICENZA	0611	A	CLINIC	N	6
AHC VILSECK	1017	A	CLINIC	N	6
AHC WIESBADEN	1147	A	CLINIC	N	10
ANDREW RADER AHC-FT. MYER	0390	A	CLINIC	Y	16
BASSETT ACH-FT. WAINWRIGHT	0005	A	HOSP	Y	30
BAYNE-JONES ACH-FT. POLK	0064	A	HOSP	Y	28
BLANCHFIELD ACH-FT. CAMPBELL	0060	A	HOSP	Y	93
BMA NAVCAMS EASTPAC	0284	N	CLINIC	Y	1
BMC ALBANY	0275	N	CLINIC	Y	1
BMC ANDREWS AFB	0522	N	CLINIC	Y	1
BMC ATHENS	0276	N	CLINIC	Y	0
BMC BARSTOW	0209	N	CLINIC	Y	1
BMC CAMP BUSH/COURTNEY	7032	N	CLINIC	N	4
BMC CAMP DELMAR MCB	1657	N	CLINIC	Y	0
BMC CAMP GEIGER MCB	1662	N	CLINIC	Y	9
BMC CAMP HANSEN	7033	N	CLINIC	N	2
BMC CAMP JOHNSON MCB	1663	N	CLINIC	Y	4
BMC CAMP KINSER	1269	N	CLINIC	N	3
BMC CAMP SCHWAB-OKINAWA	7107	N	CLINIC	N	1
BMC CAPODICHINO	1153	N	CLINIC	N	3
BMC CHESAPEAKE	0519	N	CLINIC	Y	1

Facility Name	DMIS ID	Branch of service	Facility Type	US Flag?	Avg. daily tests
BMC COMFLEACT SASEBO	0852	N	CLINIC	N	2
BMC CORCEN MCB	1975	N	CLINIC	Y	0
BMC CORONADO	0233	N	CLINIC	Y	0
BMC DAHLGREN	0386	N	CLINIC	Y	1
BMC DAM NECK	0382	N	CLINIC	Y	8
BMC EDSON RANGE ANNEX	0210	N	CLINIC	Y	12
BMC EL CENTRO	0239	N	CLINIC	Y	1
BMC EVANS-CAMP FOSTER	0862	N	CLINIC	N	4
BMC FRENCH CREEK MCB	1995	N	CLINIC	Y	5
BMC GAETA	0874	N	CLINIC	N	1
BMC INDIAN HEAD	0301	N	CLINIC	Y	2
BMC IWAKUNI	0625	N	CLINIC	N	8
BMC KEY WEST	0041	N	INACT	Y	2
BMC LITTLE CREEK	0378	N	CLINIC	Y	51
BMC MARIETTA	0277	N	CLINIC	Y	1
BMC MAYPORT	0405	N	CLINIC	Y	14
BMC MCAS BEAUFORT	0360	N	CLINIC	Y	2
BMC MCAS FUTENMA	0861	N	CLINIC	N	1
BMC MCAS KANEOHE BAY	0285	N	CLINIC	Y	8
BMC MCAS MIRAMAR	0232	N	CLINIC	Y	13
BMC MCAS NEW RIVER	0333	N	CLINIC	Y	3
BMC MCB CAMP H.M. SMITH	1987	N	CLINIC	Y	1
BMC MCB CAMP PENDLETON	0208	N	CLINIC	Y	1
BMC MCRD PARRIS ISLAND	0358	N	CLINIC	Y	30
BMC MCRD SAN DIEGO	0230	N	CLINIC	Y	16
BMC MECHANICSBURG	0348	N	CLINIC	Y	0
BMC MERIDIAN	0317	N	CLINIC	Y	3
BMC MILTON WHITING FIELD	0261	N	CLINIC	Y	5
BMC NAF ATSUGI	0853	N	CLINIC	N	9
BMC NAS JACKSONVILLE	0266	N	CLINIC	Y	4
BMC NAS MEMPHIS	0361	N	INACT	Y	2
BMC NAS NORTH ISLAND	0231	N	CLINIC	Y	7
BMC NAS PENSACOLA	0260	N	CLINIC	Y	6
BMC NAS POINT MUGU	0217	N	CLINIC	Y	1
BMC NATTC PENSACOLA	0262	N	CLINIC	Y	12
BMC NAVCOASTSYSC PANAMA CITY	0265	N	CLINIC	Y	1
BMC NAVSTA SAN DIEGO	0234	N	INACT	Y	7
BMC NAVSUPPO LA MADDALENA	0855	N	CLINIC	N	1
BMC NAVWPNCEN CHINA LAKE	0212	N	CLINIC	Y	13
BMC NAVWPNSFAC ST. MAWGAN	1179	N	CLINIC	N	0
BMC NSA BAHRAIN	1170	N	CLINIC	N	3
BMC NSY NORFOLK	0380	N	CLINIC	Y	0
BMC NTC GREAT LAKES	1959	N	CLINIC	Y	8
BMC NTC SAN DIEGO	0407	N	CLINIC	Y	13
BMC NTTC PENSACOLA	0513	N	CLINIC	Y	5
BMC OCEANA	0387	N	CLINIC	Y	20
BMC SAN ONOFRE MCB	1659	N	CLINIC	Y	2

Facility Name	DMIS ID	Branch of service	Facility Type	US Flag?	Avg. daily tests
BMC SUGAR GROVE	0404	N	CLINIC	Y	0
BMC WILLOW GROVE	0347	N	CLINIC	Y	1
BMC YORKTOWN	0381	N	CLINIC	Y	1
BMC YUMA	0269	N	CLINIC	Y	5
DEWITT ACH-FT. BELVOIR	0123	A	HOSP	Y	57
DILORENZO TRICARE HLTH CLN ARL	7298	A	CLINIC	Y	11
DSCPL BRKS HLTH CLN-FT LEAVENW	1530	A	CLINIC	Y	0
DUGWAY PROVING GROUND AHC	0371	A	CLINIC	Y	0
DUNHAM AHC-CARLISLE BARRACKS	0352	A	CLINIC	Y	17
FAMILY HEALTH CENTER FAIRFAX	6200	A	CLINIC	Y	25
FAMILY HEALTH CENTER WOODBRIDG	6201	A	CLINIC	Y	45
FOX AHC-REDSTONE ARSENAL	0001	A	CLINIC	Y	7
GUTHRIE AHC-FT. DRUM	0330	A	CLINIC	Y	37
HEIDELBERG MEDDAC	0606	A	HOSP	N	21
KENNER AHC-FT. LEE	0122	A	CLINIC	Y	15
KIMBROUGH AMB CAR CEN-FT MEADE	0069	A	CLINIC	Y	28
KIRK AHC-ABERDEEN PRVNG GD	0308	A	CLINIC	Y	15
LA POINTE HEALTH CLINIC	7307	A	CLINIC	Y	6
LANDSTUHL REGIONAL MEDCEN	0607	A	HOSP	N	48
LYSTER ACH-FT. RUCKER	0003	A	HOSP	Y	21
MARTIN ACH-FT. BENNING	0048	A	HOSP	Y	131
MCDONALD ACH-FT. EUSTIS	0121	A	HOSP	Y	70
MENWITH HILL MEDICAL CENTER	7234	F	CLINIC	N	0
MONCRIEF ACH-FT. JACKSON	0105	A	HOSP	Y	60
MONROE AHC-FT. MONROE	0372	A	CLINIC	Y	2
MONTEREY AHC	0247	A	CLINIC	Y	1
MUNSON AHC-FT. LEAVENWORTH	0058	A	CLINIC	Y	19
NACC KINGS BAY	0337	N	CLINIC	Y	5
NAS NORFOLK NRMC/BC	0377	N	CLINIC	Y	28
NH BEAUFORT	0104	N	HOSP	Y	37
NH CAMP LEJEUNE	0091	N	HOSP	Y	120
NH CAMP PENDLETON	0024	N	HOSP	Y	48
NH CHARLESTON	0103	N	HOSP	Y	13
NH CHERRY POINT	0092	N	HOSP	Y	60
NH GREAT LAKES	0056	N	HOSP	Y	47
NH GUAM-AGANA	0620	N	HOSP	Y	25
NH JACKSONVILLE	0039	N	HOSP	Y	36
NH KEFLAVIK	0623	N	HOSP	N	4
NH NAPLES	0617	N	HOSP	N	20
NH OKINAWA	0621	N	HOSP	N	30

Facility Name	DMIS ID	Branch of service	Facility Type	US Flag?	Avg. daily tests
NH PENSACOLA	0038	N	HOSP	Y	92
NH TWENTYNINE PALMS	0030	N	HOSP	Y	26
NH YOKOSUKA	0622	N	HOSP	N	38
NMC PORTSMOUTH	0124	N	HOSP	Y	80
NMC SAN DIEGO	0029	N	HOSP	Y	139
NMCL ANNAPOLIS	0306	N	CLINIC	Y	13
NMCL LONDON	8931	N	CLINIC	N	2
NMCL PATUXENT RIVER	0068	N	CLINIC	Y	12
NMCL PEARL HARBOR	0280	N	CLINIC	Y	28
NMCL QUANTICO	0385	N	CLINIC	Y	29
NNMC BETHESDA	0067	N	HOSP	Y	85
OP FORCES-NH GREAT LAKES	6308	N	ADMIN	Y	20
RECEPTION STA TMC-FT. BENNING	1939	A	CLINIC	Y	1
REYNOLDS ACH-FT. SILL	0098	A	HOSP	Y	95
RICHARDS-GEBAUR CL-KANSAS CITY	7297	A	CLINIC	Y	3
SCHOFIELD BARRACKS AHC	0437	A	CLINIC	Y	28
SGT BLEAK TROOP MED CLN-FT SIL	1625	A	CLINIC	Y	8
SOUTHCOM CLINIC	7239	A	CLINIC	Y	0
TMC CON (1-2-4)-FT. JACKSON	1567	A	CLINIC	Y	19
TMC FT. RICHARDSON	0204	A	CLINIC	Y	1
TMC-1-FT. BENNING	1551	A	CLINIC	Y	2
TMC-1-FT. STEWART	1562	A	CLINIC	Y	5
TMC-1-SCHOF 25th-SCHOFIELD BKS	0534	A	CLINIC	Y	8
TMC-2-FT. BENNING	1552	A	CLINIC	Y	2
TMC-5-FT. BENNING	1555	A	CLINIC	Y	4
TMC-7-FT. BENNING	1557	A	CLINIC	Y	3
TOOELE ARMY DEPOT AHC	0443	A	CLINIC	Y	0
TRICARE OUTPATIENT CHESAPEAKE	6221	N	CLINIC	Y	16
TRICARE OUTPATIENT CL VA BEACH	6214	N	CLINIC	Y	33
TRICARE OUTPATIENT-CHULA VISTA	6215	N	CLINIC	Y	19
TRICARE OUTPATIENT-CLAIRMONT	6207	N	CLINIC	Y	18
TRICARE OUTPATIENT-OCEANSIDE	6216	N	CLINIC	Y	6
TRIPLER AMC-FT SHAFTER	0052	A	HOSP	Y	101
TUTTLE AHC-HUNTER AB	0272	A	CLINIC	Y	15
USA MEDDAC-CAMP ZAMA	0610	A	CLINIC	N	6
WALTER REED AMC-WASHINGTON DC	0037	A	HOSP	Y	99
WILLIAM BEAUMONT AMC-FT. BLISS	0108	A	HOSP	Y	48
WINDER FPC-FT. BENNING	1316	A	CLINIC	Y	17
WINN ACH-FT. STEWART	0049	A	HOSP	Y	103
WUERZBURG MEDDAC	0609	A	HOSP	N	16

Appendix 3: DoD-ESSENCE ICD-9 Syndrome Definitions

Syndrome=Bot-like

icd9	Dx
005.1	Botulism
038.2	Septicemia, pneumococcal
344.00	Quadriplegia, Unspec.
344.04	Quadriple/Quadripa.C5-C7
344.09	Quadriplegia/Quadriparesis
344.2	Diplegia of upper limbs
344.89	Paralytic Syndrome, Other
344.9	Paralysis
351.8	Neuralgia, Facial
351.9	Facial Nerve Disorder, Unspec
352.6	Cranial Nerve Palsies, Mult.
352.9	Cranial Nerve Disorder, Unspec
368.2	Diplopia
374.30	Ptosis of Eyelid, Unspec.
374.31	Paralytic Ptosis
378.51	Nerve Palsy, 3rd Or Oculomotor, Partial
378.52	Nerve Palsy, 3rd Or Oculomotor, Total
784.3	Aphasia

Syndrome=Fever

icd9	Dx
038.8	Septicemia NEC
038.9	Septicemia NOS
066.1	Fever, tick-borne
066.3	Fever, mosquito-borne NEC
066.8	Disease, arthpd-borne viral NEC
066.9	Disease, arthpd-borne viral NOS
078.2	Sweating fever
079.89	Infection, viral NEC
079.99	Infection, viral NOS
780.31	Convulsions, febrile
780.6	Fever
790.7	Bacteremia
790.8	Viremia NOS
795.39	NONSP POSITIVE CULT NEC

Syndrome=GI

icd9	Dx
001.0	Cholera d/t Vibrio cholerae
001.1	Cholera d/t Vibrio cholerae el tor
001.9	Cholera NOS
003.0	Gastroenteritis, salmonella
003.8	Infection, salmonella NEC

003.9	Infection, salmonella NOS
004.0	Dysentery, Shigella dysenteriae
004.1	Dysentery, Shigella flexneri
004.2	Dysentery, Shigella boydii
004.3	Dysentery, Shigella sonnei
004.8	Infection, Shigella NEC
004.9	Shigellosis NOS
005.0	Poisoning, food, staphylococcal
005.2	Pois, food, d/t C. perfringens
005.3	Pois, food, d/t clostridia NEC
005.4	Pois, food, d/t v. parahaemolyt
005.81	Pois, food, d/t Vibrio vulnificus
005.89	Poisoning, food, bacterial NEC
005.9	Poisoning, food NOS
007.5	CYCLOSPORIASIS
008.00	Enteritis, E. coli NOS
008.01	Enteritis, enteropathogenic E. coli
008.02	Enteritis, enterotoxigenic E. coli
008.03	Enteritis, enteroinvasive E. coli
008.04	Enteritis, enterohemorrhagic E.coli
008.09	Enteritis, E. coli NEC
008.1	Enteritis, Arizona group
008.2	Enteritis, Aerobacter aerogenes
008.3	Enteritis, Proteus
008.41	Enteritis, staphylococcus
008.43	Enteritis, Campylobacter
008.44	Enteritis, Yersinia enterocolitica
008.45	Enteritis, Clostridium difficile
008.46	Enteritis, anaerobic NEC
008.47	Enteritis, gram-negative NEC
008.49	Enteritis, bacterial NEC
008.5	Enteritis, bacterial NOS
008.61	Enteritis d/t rotavirus
008.62	Enteritis d/t adenovirus
008.63	Enteritis d/t Norwalk virus
008.64	Enteritis d/t small round virus NEC
008.65	Enteritis d/t calcivirus
008.66	Enteritis d/t astrovirus
008.67	Enteritis d/t enterovirus NEC
008.69	Enteritis d/t virus NEC
008.8	Enteritis, viral NOS
009.0	Enteritis, infectious NOS
009.1	Enteritis presumed infct origin
009.2	Diarrhea, infectious
009.3	Diarrhea, presumed infct origin
021.1	Tularemia, enteric
022.2	Anthrax, gastrointestinal
078.82	Syndrome, epidemic vomiting
535.00	Gastritis, acute w/o hemorrhage
535.01	Gastritis, acute w/hemorrhage
535.40	Gastritis NEC w/o hemorrhage
535.41	Gastritis NEC w/hemorrhage
535.50	Gastritis NOS w/o hemorrhage
535.51	Gastritis NOS w/hemorrhage
535.60	Duodenitis w/o hemorrhage
535.61	Duodenitis w/hemorrhage
536.2	Vomiting, persistent

555.0	Enteritis, regional small intestine
555.1	Enteritis, regional large intestine
555.2	Enteritis, regional both intestines
558.2	Gastroenteritis/colitis, toxic
558.9	Gastroenteritis, noninfct NEC
569.9	Disorder, intestinal NOS
787.01	Nausea with vomiting
787.02	Nausea alone
787.03	Vomiting alone
787.3	Flatulence/eructation/gas pain
787.91	Diarrhea NOS

Syndrome=Hemr_ill

icd9	Dx
065.0	Hemorrhagic fever, Crimean
065.1	Hemorrhagic fever, Omsk
065.2	Kyasanur Forest disease
065.3	Hemorrhagic fever, tick-borne NEC
065.4	Hemorrhagic fever, mosquito-borne
065.8	Hemorrhagic fever, arthpd-borne NEC
065.9	Hemorrhagic fever, arthpd-borne NOS
077.4	Conjunctivitis, epidemic hem
078.6	Nephrosonephritis, hemorrhagic
078.7	Hemorrhagic fever, arenaviral
084.8	Fever, blackwater
100.0	Leptospirosis icterohemorrhagica
283.11	Syndrome, hemolytic-uremic
286.9	Defect, coagulation NEC/NOS
287.1	Thrombocytopathy
287.2	Purpura NOS
287.3	Thrombocytopenia, primary
287.4	Thrombocytopenia, secondary
287.5	Thrombocytopenia NOS
287.8	Hemorrhagic condition NEC
287.9	Hemorrhagic condition NOS
459.0	Hemorrhage NOS
782.7	Ecchymoses, spontaneous
790.01	Hematocrit, Precipitous Drop
790.92	Abnormal blood coagulation profile

Syndrome=Neuro

icd9	Dx
003.21	Meningitis, salmonella
036.0	Meningitis, meningococcal
036.1	Encephalitis, meningococcal
037	Tetanus
047.0	Meningitis d/t Coxsackie virus
047.1	Meningitis d/t ECHO virus
047.8	Meningitis, viral NEC
047.9	Meningitis, viral NOS
048	Disease, enteroviral of CNS NEC

049.0	Choriomeningitis, lymphocytic
049.1	Meningitis, adenovirus
049.8	Encephalitis, viral NEC
049.9	Encephalitis, viral NOS
052.0	Encephalitis, postvaricella
053.0	Herpes zoster w/meningitis
053.10	Herpes zoster w/nrv syst cmpl NOS
054.3	Herpetic meningoencephalitis
054.72	Herpes simplex meningitis
055.0	Encephalitis, postmeasles
056.00	Rubella w/neurological cmpl NOS
056.01	Encephalomyelitis d/t rubella
056.09	Rubella w/neurological cmpl NEC
062.0	Encephalitis, Japanese
062.1	Encephalitis, Western equine
062.2	Encephalitis, Eastern equine
062.3	Encephalitis, St. Louis
062.4	Encephalitis, Australian
062.5	Encephalitis, California virus
062.8	Encephalitis, mosquito-borne NEC
062.9	Encephalitis, mosquito-borne NOS
063.0	Encephalitis, Russian spring-summer
063.1	Louping ill
063.2	Encephalitis, central European
063.8	Encephalitis, viral, tick-borne NEC
063.9	Encephalitis, tick-borne viral NOS
064	Encephalitis arthpd-borne viral NEC
066.4	WEST NILE FEVER
072.1	Mumps meningitis
072.2	Mumps encephalitis
091.81	Syph meng, early, symp, acute, scnd
098.82	Meningitis, gonococcal
100.81	Meningitis (aseptic), leptospiral
114.2	Coccidioidal meningitis
115.01	Histoplasma capsulatum meningitis
115.11	Histoplasma duboisii meningitis
115.91	Histoplasmosis meningitis
130.0	Meningoencephalitis, toxoplasmosis
320.0	Meningitis, Hemophilus
320.1	Meningitis, pneumococcal
320.2	Meningitis, streptococcal
320.3	Meningitis, staphylococcal
320.7	Meng, in oth bctrl disease CE
320.81	Meningitis, d/t anaerobic bacteria
320.82	Meng, d/t gram-negative bact NEC
320.89	Meningitis, d/t other spec bacteria
320.9	Meningitis, d/t bacteria NOS
321.0	Meningitis, cryptococcal
321.1	Meningitis in other fungal disease
321.2	Meningitis d/t viral diseases NEC
321.3	Meningitis d/t trypanosomiasis
321.4	Meningitis in sarcoidosis
321.8	Meng d/t oth nonbact organism CE
322.0	Meningitis, nonpyogenic
322.1	Meningitis, eosinophilic
322.9	Meningitis NOS
323.0	Encephalitis in viral disease CE

323.1	Encephalitis in rickettsial dis CE
323.2	Encephalitis in protozoal dis CE
323.4	Encephalitis, oth d/t infection CE
323.5	Encephalitis, postimmunization
323.6	Encephalitis, postinfectious
323.7	Encephalitis, toxic
323.8	Encephalitis NEC
323.9	Encephalitis NOS
348.30	Encephalopathy NOS
348.39	Encephalopathy NEC
781.6	Meningismus

Syndrome=Rash

icd9	Dx
050.0	Smallpox, variola major
050.1	Smallpox, alastrim
050.2	Smallpox, modified
050.9	Smallpox NOS
051.0	Cowpox
051.1	Pseudocowpox
051.2	Dermatitis, contagious pustular
051.9	Paravaccinia NOS
052.7	Varicella complication NEC
052.8	Varicella complication NOS
052.9	Varicella uncomplicated
055.79	Measles w/complication NEC
055.8	Measles w/complication NOS
055.9	Measles uncomplicated
056.79	Rubella w/complication NEC
056.8	Rubella w/complication NOS
056.9	Rubella uncomplicated
057.0	Erythema infectiosum
057.8	Exanthemata, viral NEC
057.9	Exanthemata, viral NOS
074.3	Hand, foot and mouth disease
082.0	Fever, spotted
083.2	Rickettsialpox
695.0	Erythema, toxic
695.1	Erythema multiforme
695.2	Erythema nodosum
695.89	Erythematous conditions NEC
695.9	Erythematous condition NOS

Syndrome=Resp

icd9	Dx
003.22	Pneumonia, salmonella
020.3	Plague, primary pneumonic
020.4	Plague, secondary pneumonic
020.5	Plague, pneumonic NOS
021.2	Tularemia, pulmonary
022.1	Anthrax, pulmonary

031.0	Disease, pulmonary d/t mycobacteria
031.8	Disease, mycobacterial NEC
031.9	Disease, mycobacterial NOS
032.0	Diphtheria, faucial
032.1	Diphtheria, nasopharyngeal
032.2	Diphtheria, anterior nasal
032.3	Diphtheria, laryngeal
032.89	Diphtheria NEC
032.9	Diphtheria NOS
033.0	Whoopcough, Bordetella pertussis
033.1	Whoopcough Bordetella parapertussis
033.8	Whooping cough NEC
033.9	Whooping cough NOS
034.0	Sore throat, streptococcal
052.1	Varicella pneumonitis
055.1	Pneumonia, postmeasles
055.2	Otitis media, postmeasles
073.0	Ornithosis w/pneumonia
079.0	Infection, adenovirus
079.1	Infection, ECHO virus
079.2	Infection, Coxsackie virus
079.3	Infection, rhinovirus
079.6	Infct, respiratory syncytial virus
079.82	SARS ASSOC CORONAVIRUS
381.00	OM, acute nonsuppurative NOS
381.01	OM, acute serous
381.03	OM, acute sanguinous
381.04	OM, acute allergic serous
381.4	OM, chronic nonsuppurative NOS
381.50	Salpingitis, Eustachian NOS
381.51	Salpingitis, acute Eustachian
382.00	OM, acute suppurative NOS
382.01	OM, acute suppurative w/drum rup
382.02	OM, acute suppurative in disease CE
382.4	OM, suppurative NOS
382.9	Otitis media NOS
460	Nasopharyngitis, acute
461.0	Sinusitis, acute maxillary
461.1	Sinusitis, acute frontal
461.2	Sinusitis, acute ethmoidal
461.3	Sinusitis, acute sphenoidal
461.8	Sinusitis, acute NEC
461.9	Sinusitis, acute NOS
462	Pharyngitis, acute
463	Tonsillitis, acute
464.00	Laryngitis, Acute. w/o obstruction
464.01	Laryngitis, Acute.W/ obstruction
464.10	Tracheitis, acute, w/o obstruction
464.11	Tracheitis, acute w/obstruction
464.20	Laryngotracheitis, acute w/o obst
464.21	Laryngotracheitis, acute w/obst
464.30	Epiglottitis, acute w/o obst
464.31	Epiglottitis, acute w/obstruction
464.4	Croup
464.50	Supraglottis, uns. w/out obstr.
464.51	Supraglottis, uns. w/ obstr.
465.0	Laryngopharyngitis, acute

465.8	Infct up rsprt mlt sites, acute NEC
465.9	Infct up rsprt mlt sites, acute NOS
466.0	Bronchitis, acute
466.11	Bronchiolitis, acute, d/t RSV
466.19	Bronchio acute d/t oth infct orgnsm
478.9	Disease, upper respiratory NEC/NOS
480.0	Pneumonia, adenovirus
480.1	Pneumonia d/t rsprt syncytial virus
480.2	Pneumonia d/t parainfluenza virus
480.3	PNEUMONIA DUE TO SARS
480.8	Pneumonia d/t virus NEC
480.9	Pneumonia d/t virus NOS
481	Pneumonia d/t pneumococcal virus
482.0	Pneumonia d/t Klebsiella pneumoniae
482.1	Pneumonia d/t Pseudomonas
482.2	Pneumonia d/t Hemophilus influenzae
482.30	Pneumonia d/t Streptococcus NOS
482.31	Pneumonia d/t Streptococcus Group A
482.32	Pneumonia d/t Streptococcus Group B
482.39	Pneumonia d/t Streptococcus NEC
482.40	Pneunonia d/t Staphylococcus NOS
482.41	Pneumonia d/t Staphylococcus aureus
482.49	Pneumonia d/t Staphylococcus NEC
482.81	Pneumonia d/t anaerobes
482.82	Pneumonia d/t Escherichia coli
482.83	Pneumonia d/t gram-negative NEC
482.84	Pneumonia d/t Legionnaires' disease
482.89	Pneumonia, bacterial NEC
482.9	Pneumonia, bacterial NOS
483.0	Pneumonia d/t Mycoplasma pneumoniae
483.1	Pneumonia d/t Chlamydia
483.8	Pneumonia d/t organism NEC
484.1	Pneumonia in cytomegalic incls dis
484.3	Pneumonia in whooping cough
484.5	Pneumonia in anthrax
484.6	Pneumonia in aspergillosis
484.7	Pneumonia in systemic mycoses
484.8	Pneumonia in oth infct disease CE
485	Bronchopneumonia, organism NOS
486	Pneumonia, organism NOS
487.0	Influenza w/pneumonia
487.1	Influenza w/rsprt mnfst NEC
487.8	Influenza w/manifestation NEC
490	Bronchitis NOS
494.1	BRONCHIECTASIS W AC EXAC
511.0	Pleurisy w/o effusion or TB
511.1	Pleurisy, w/bctrl effusion, not TB
511.8	Pleurisy, effusion NEC, not TB
511.9	Effusion, pleural NOS
513.0	Abscess, lung
513.1	Abscess, mediastinum
514	Congestion/hypostasis, pulmonary
517.3	ACUTE CHEST SYNDROME
518.0	Collapse, pulmonary
518.4	Edema, acute lung NOS
518.81	Failure, acute respiratory
518.82	Insufficiency, pulmonary NEC

518.84	Respiratory failure,acute & chronic
519.2	Mediastinitis
519.3	Disease, mediastinum NEC
769	Syndrome, respiratory distress
782.5	Cyanosis
784.1	Pain, throat
786.00	Abnormality, respiratory NOS
786.05	Shortness of breath
786.06	Tachypnea
786.07	Wheezing
786.09	Abnormality, respiratory NEC
786.1	Stridor
786.2	Cough
786.3	Hemoptysis
786.52	Painful respiration
786.7	Abnormal chest sounds
786.9	Symp inv respiratory syst/chest NEC

Syndrome=Shk-Coma

icd9	Dx
040.82	TOXIC SHOCK SYNDROME
458.9	Hypotension NOS
780.01	Coma
785.50	Shock NOS
785.52	SEPTIC SHOCK
785.59	Shock w/o trauma NEC
798.1	Death, instantaneous
798.2	Death, less than 24 hrs onset symp
798.9	Death, unattended
799.1	Arrest, respiratory

Appendix 4: DoD synonyms for test names

New Test Name	New Print Name	Synonym
ACANTHAMOEBA CULTURE	ACANTHAM CULT	CULTURE ACANTHAMOEBA
ACANTHAMOEBA/NAEGLERIA CULT	ACANTH/NAEG	CULTURE ACANTHAMEOBA/NAEGLERIA
ACTIN THERMOPHILIC COLONY CT	ACTIN THERMOPHI	
AEROBIC CULTURE	AEROBIC CULT	AEROBIC BLOOD CULT; AEROBIC BC; A BC; AEROBIC BODY FLUID CULT; AEROBIC BF CULT; A BF CULTURE; CULTURE AEROBIC
ANAEROBIC CULTURE	ANAER CULT	ANAEROBIC BLOOD CULT; ANAEROBIC BC; ANA BC; ANAEROBIC BODY FLUID CULT; ANAEROBIC BF CULT; ANA BF CULTURE; CULTURE ANAEROBIC
B ANTHRACIS BETAPHAGE	ANTHRAX PHAGE	BACILLUS ANTHRACIS; ANTHRAX PHAGE
B ANTHRACIS CULTURE	ANTHRAX CULT	BACILLUS ANTHRACIS; ANTHRAX CULTURE; CULTURE, ANTHRAX
B ANTHRACIS DFA	ANTHRAX DFA	BACILLUS ANTHRACIS; ANTHRAX DFA
B ANTHRACIS ID	B ANTHRACIS ID	ANTHRAX
B ANTHRACIS PCR	ANTHRAX PCR	BACILLUS ANTHRACIS; ANTHRAX PCR
B BURGDORFERI	B BURGDORFERI	LYMES DISEASE
B DERMATITIDIS EXO-AG ID	B DERM EXO-AG	
B HENSELAE CULTURE	B HENSELAE CULT	BARTONELLA HENSELAE CULTURE
B HENSELAE H-1	B HENSELAE H-1	B HENSELAE H1; BARTONELLA HENSELAE H-1
B PERTUSSIS CULTURE	PERTUSSIS CULT	BORDETELLA PERTUSSIS CULTURE
B QUINTANA OK	B QUINTANA OK	B QUINTANA OKLAHOMA
BACTERIA	BACTERIA	CULTURE, BACTERIA
BACTERIA ID GAS CHROM	BACTERIA ID GC	
BACTERIA ID PFGE	BACTERIA ID PFG	
BARTONELLA CULTURE	BARTON CULT	CULTURE BARTONELLA
BETA STREP ALLERGIC	STREP ALLERGIC	STREPTOCOCCUS B PCN ALLERGIC; BETA STREP-PCN ALLERGIC
BLASTOMYCES ID	BLASTO ID	BLASTOMYCOSIS
BLOOD CULTURE	BLD CULT	BC; PED BC; PEDIATRIC BLOOD CULTURE; CULTURE BLOOD
BLOOD CULTURE ANAEROBIC	BLD CULT ANA	BC ANAEROBIC; ANAEROBIC BLOOD CULTURE
BODY FLUID CULT	BF CULT	BF CULTURE; CULTURE BODY FLUID

BORDETELLA CULTURE	BORDETELLA CULT	WHOOPING COUGH
BORDETELLA PERTUSSIS	B PERTUSSIS	WHOOPING COUGH; BORDETELLA PERTUSSIS CULTURE
BORDETELLA SP CULTURE	BORDTELA S CULT	BORDETELLA SP CULTURE
BORDETELLA SP ID	BORDETEL SP ID	
BORRELIA SP CULTURE	BORRELIA S CULT	BORRELIA SP CULTURE
BORRELIA SP ID	BORRELIA SP ID	
BRUCELLA CULTURE	BRUCELLA CULT	BRUCELLOSIS
BURKHOLDERIA CULTURE	BURKHOLD CULT	
C DIFFICILE	C DIFFICILE	CLOSTRIDIUM DIFFICILE
C DIPHTHERIAE CULTURE	C DIPHTHER CULT	CLOSTRIDIUM DIPHTHERIA; CORYNEBACTERIUM DIPHTHERIAE
C TRACHOMATIS	C TRACHOMATIS	CHLAMYDIA TRACHOMATIS
CALYMMATOBACTERIUM GRANULOMTIS	C GRANULOMTIS	
CAMPYLOBACTER ID	CAMPY ID	
CAMPYLOBACTER SP ID	CAMPY SP ID	
CATALASE TEST	CATALASE	
CERVICAL MUCUS	CERVICAL MUCUS	
CHLAMYDIA CULTURE	CHLAMYDIA CULT	
CHLAMYDIA SP IDENTIFIED	CHLAMYDIA SP ID	CHLAMYDIA SP ID
CHLORACETATE ESTERASE STAIN	CE STAIN	
CLO TEST	CLO TEST	
CLOTEST	CLOTEST	H PYLORI; HELICOBACTER PYLORI
COCCI IMMITIS EXOAG ID	C IMMITIS EXOAG	
COCCIDIOIDES ID	COCCIDIA ID	
COCCIDIOIDES IDCF ID	COCCIDIO IDCF	
COCCIDIOIDES IDTP ID	COCCIDIO IDTP	
COLONY COUNT	COLONY COUNT	
CRYPTOSPORIDIUM	CRYPTOSPORIDIUM	
CSF CULT	CSF CULTURE	CULTURE CSF; SPINAL FLUID CULTURE
CYANOBACTERIUM ID	CYANOBTERIUM ID	
CYCLOSPORA CYAETINESUS	C CYAETINESUS	
CYCLOSPORA ID	CYCLOSPORA ID	
DIPHTHERIA SP ID	DIPHTHERIA SP	
E COLI ENTERO ID	E COLI ENTER ID	ESCHERICHIA COLI ENTEROHEMORRHAGIC ID
E COLI O157:H7	E COLI O157:H7	ESCHERICHIA COLI O157:H7
E COLI O157:H7 ID	E COLI O157:H7	ESCHERICHIA COLI O157:H7 ID
E TEST	E TEST	E TEST SUSCEPTIBILITY; SUSCEPTIBILITY
EAR CULTURE	EAR CULT	CULTURE EAR
ENTEROVIRUS ID	ENTEROVIRUS ID	
ENVIRON CULT BT	ENVIRON CULT BT	
EYE CULTURE	EYE CULT	CULTURE EYE

F TULARENSIS CULTURE	TULARENSIS CULT	TULAREMIA
GC CULT	GC CULT	N GONORRHOEAE; GC; NEISSERIA GONORRHOEAE; GONORRHEA CULTURE
GC SMEAR	GC SMEAR	N GONORRHOEAE; GC; NEISSERIA GONORRHOEAE
GENITAL CULTURE	GENITAL CULTURE	CULTURE GENTIAL
GRAM STAIN	GRAM STAIN	
H PYLORI CULTURE	H PYLORI CULT	H PYLORI CULTURE; CAMPYLOBACTER PYLORI CULTURE; HELICOBACTER PYLORI CULTURE
HAEMOPHILUS B CULTURE	HAEMOPH B CULT	HAEMOPHILUS B CULTURE
HAEMOPHILUS DUCREYI CULTURE	H DUCREYI CULT	H DUCREYI CULTURE
HAEMOPHILUS SP IDENTIFIED	HAEMOPHIL SP ID	HAEMOPHILUS SP ID
HISTOPLASMA CULTURE	HISTOPLASM CULT	
LEGIONELLA CULTURE	LEGIONELLA CUL	LEGIONELLA
LEGIONELLA SP	LEGIONELLA SP	
LEGIONELLA SP IDENTIFIED	LEGION SP ID	LEGIONELLA SP ID
LEPTOSPIRA SP ID	LEPTOSPIR SP ID	
LISTERIA SP ID	LISTERIA SP ID	
M HOMINIS	M HOMINIS	MYCOPLASMA HOMINIS
M PNEUMONIAE CULTURE	M PNEUMO CULT	MYCOPLASMA PNEUMONIAE CULTURE
METH RESISTANT S AUREUS	MRSA	MRSA
MICROORGANISM IDENTIFIED	MICROORG ID	MICROORGANISM ID
MYCOPLASMA SP GENITAL ID	MYCOPLAS GENITA	MYCOPLASMA SP GENITAL ID
MYCOPLASMA SP IDENTIFIED	MYCOPLASM SP ID	MYCOPLASMA SP ID
MYCOPLASMA SP RESP ID	MYCOPLAS RESP	MYCOPLASMA SP RESP ID
MYCOPLASMA/UREAPLASMA CUL	MYCOPLASMA CULT	
MYCOPLASMA+UREAPLASMA SP	MYCOPLASMA+UREA	
N GONORRHOEAE	N GONORRHOEAE	N GONORRHOEAE; GC; NEISSERIA GONORRHOEAE
NASAL CULTURE	NASAL CULT	CULTURE NASAL
NORMAL SALINE	SALINE	SALINE
ORGANISM COUNT	ORGANISM CNT	
ORGANISM IDENTIFICATION	ORGANISM ID	
RECTAL CULTURE	RECTAL CULT	CULTURE RECTAL
RESPIRATORY CULTURE	RESP CULT	CULTURE RESPIRATORY, NASOPHARYNGEAL CULTURE
SALMONELLA SEROGROUP	SALMONELLA GRP	
SEROTYPING H INFLUENZAE	TYPING H FLU	TYPE/GROUP H INFLUENZAE; H INFLUENZAE SEROTYPING
SEROTYPING N MENINGITIS	TYPING N MEN	TYPE/GROUP N MENINGITIS; N MENINGITIS SEROTYPING
SEROTYPING OTHER ORGANISM	TYPING OTHER	TYPE/GROUP OTHER ORGANISM

SEROTYPING STAPH AUREUS	TYPING SA	TYPE/GROUP STAPH AUREUS; STAPH AUREUS SEROTYPING
SEROTYPING STREPTOCOCCUS	TYPING STREP	TYPE/GROUP STREPTOCOCCUS; STREPTOCOCCUS SEROTYPING
SEROTYPING VIBRIO	TYPING VIBRIO	TYPE/GROUP VIBRIO; VIBRIO SEROTYPING
SHIGELLA SEROTYPE	SHIGELLA SERO	RAST; ALLERGEN
SPORE STRIP	SPORE STRIP	ATTEST
SPUTUM CULTURE	SPUTUM CULT	CULTURE SPUTUM
STERILITY TEST	STERILITY TEST	
STOOL CULTURE	STOOL CULT	CULTURE STOOL
STREP AGALACTIAE ID	S AGALACTIAE ID	
STREPTOCOCCUS B-HEMOLYTIC	STREP B-HEMOLY	BETA HEMOLYTIC STREPTOCOCCUS
SUSCEPTIBILITY AEROBIC	SUSC AER	AEROBIC SUSCEPTIBILITY
SUSCEPTIBILITY ANAEROBIC	SUSC ANA	ANAEROBIC SUSCEPTIBILITY
TARCROLINUS	TARCROLINUS	
THROAT CULTURE	THR CULT	TC; CULTURE THROAT
TISSUE CULTURE	TISSUE CULT	CULTURE TISSUE
TOXOPLASMA SP	TOXOPLASMA SP	
TOXOPLASMA SP ID	TOXOPLASM SP ID	
UREAPLASMA UREALYTICUM CULT	U UREALYTICUM	
URINE CULTURE	UA CULT	UC; CULTURE URINE
VANCO INTERMED S AUREUS	VISA	VISA
VANCO RESIST ENTEROCOCCUS	VRE ID	VANCOMYCIN RESISTANT ENTEROCOCCUS; VRE SCREEN
VANCO RESIST S AUREUS	VRSA	VRSA
VIBRIO SP ID	VIBRIO SP ID	
WATER CULTURE	H20 CULT	CULTURE WATER
WOUND CULTURE	WND CULT	WC; SUPERFICIAL WOUND; SUPERFICIAL WND CULT; ABSCESS CULTURE
WOUND CULTURE DEEP	DP WND CULT	DEEP WND CULTURE; DEEP WND CULT; DEEP WC; CULTURE WOUND
YERSINIA CULTURE	YERSINIA CULT	

Appendix 5: Standardized Test Names

Laboratory test order classification

std_test_ord	tstorder	COUNT	PERCENT
ACINETOBACTER	ACINETO SCREEN	8	0.000
AER BLD CULT	AERO BC	255	0.014
	AERO BLD CULT	660	0.037
	AEROBIC BC	607	0.034
	AEROBIC BLD	469	0.026
	AEROBIC BLD CUL	1353	0.076
	AEROBIC CULT,BLOOD	224	0.013
	AEROBIC CULTURE,BLOOD	228	0.013
	BC (AER)	3248	0.182
	BC AER	92	0.005
	BLD CULT, AEROB	695	0.039
	BLD,AEROBIC	3520	0.197
	BLOOD CX,AERO	833	0.047
	C AEROBIC BLD	667	0.037
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AER BLD CULT		12851	0.720
AEROBIC CULT	AER CULT	200	0.011
	AEROBIC CULT	10095	0.566
	AEROBIC CULTURE	732	0.041
	C AEROBIC	3077	0.172
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AEROBIC CULT		14104	0.790
AFB	ACID FAST CULT	2	0.000
	AFB	2	0.000
	AFB BC	1	0.000
	AFB BLD CX	5	0.000
	AFB CONC	22	0.001
	AFB CUL BLOOD	9	0.001
	AFB CULT	7997	0.448
	AFB CULTURE	522	0.029
	AFB ID	1	0.000
	AFB PAN-APATH	50	0.003
	AFB PANEL	1068	0.060
	AFB SMEAR	15	0.001
	AFB SMEAR/CULTU	54	0.003
	AFB SMR AURAMIN	82	0.005
	AFB SMR KINYOUN	1	0.000
	AFB SMR/CULT	450	0.025
	AFB SPUTUM	5	0.000
	AFB ST/CULT	5	0.000
	AFB STAIN	111	0.006
	AFB STAIN/CUL	11	0.001
	AFB-BNH	5	0.000
	BLD CULT-CAFB	19	0.001
	C AFB	182	0.010
	MYCO (WBG)	1	0.000
	MYCOBTER ID	108	0.006
	TB CULT	6	0.000
	TB ISO BLD CULT	10	0.001
	WBC-CAFB	21	0.001

Laboratory test order classification

std_test_ord	tstorder	COUNT	PERCENT
AFB		10765	0.603
ANAER BLD CULT	ANA BC	3	0.000
	ANA BLD	7	0.000
	ANAER CULT,BLOOD	181	0.010
	ANAEROBBLD CULT	651	0.036
	ANAEROBIC BC	393	0.022
	ANAEROBIC BLD	465	0.026
	ANAEROBIC CULT,BLOOD	6	0.000
	ANAEROBIC CULTU,BLOOD	1	0.000
	BC ANA	1079	0.060
	BLD CULT,ANAERO	600	0.034
	BLD,ANAEROBIC	995	0.056
	BLOOD CX ANA	787	0.044
ANAER BLD CULT		5168	0.290
ANAER CULT	ANA CULT	62	0.003
	ANAER CULT	3234	0.181
	ANAER CX	1	0.000
	ANAEROB	6	0.000
	ANAEROBE CULTUR	51	0.003
	ANAEROBE-APATH	91	0.005
	ANAEROBIC C&S	113	0.006
	ANAEROBIC CULT	223	0.012
	ANAEROBIC CX	11	0.001
	ANAEROBIC PANEL	1438	0.081
	C ANAEROBIC	515	0.029
ANAER CULT		5745	0.322
BF CULT	AER CULT,BF	12	0.001
	AEROBIC CULT,BF	759	0.043
	ANA CULT,BF	12	0.001
	ANAER CULT,BF	70	0.004
	ANAEROBIC PANEL,BF	3	0.000
	BDY FLD	4	0.000
	BDY FLD CULTURE	129	0.007
	BF CULT	1175	0.066
	BF CX	14	0.001
	BODY FL CULTURE	31	0.002
	BODY FLUID	174	0.010
	BODY FLUID CUL	8	0.000
	BODY FLUID CULT	420	0.024
	C BODY FLUID	405	0.023
	C&S BDY FLD OTH	1138	0.064
	CUL BODY FLUID	48	0.003
	CULTURE,BF	79	0.004
	FL C&S	26	0.001
	FLD CULT	39	0.002
	FLUID	23	0.001
	FLUID C&S	148	0.008

Laboratory test order classification

std_test_ord	tstorder	COUNT	PERCENT
BF CULT	FLUID CULT	2665	0.149
	FLUID CULTURE	225	0.013
	MISC CULTURE,BF	9	0.001
	SBF CULTURE	4	0.000
	STERILE SITE CX	778	0.044
	STERILE SITEC&S	1	0.000
	SYN CUL	2	0.000
	SYNOVIAL CX,BEN	3	0.000
BF CULT		8404	0.471
BLD CULT	ADULT BLD CULT	11	0.001
	BC A/AN	385	0.022
	BC AER & ANAER	67	0.004
	BC PED AER	176	0.010
	BC SET	35	0.002
	BC W/RES	212	0.012
	BLD CLT ANA/AER	476	0.027
	BLD CULT	109107	6.113
	BLD CULT PANEL	766	0.043
	BLD CULT SET	191	0.011
	BLD CULT,ADULT	349	0.020
	BLD CX	804	0.045
	BLOOD CUL	1834	0.103
	BLOOD CULT PEDI	225	0.013
	BLOOD CULTURE	10399	0.583
	BLOOD CULTURE P	718	0.040
	BLOOD CX	1647	0.092
	BLOOD CX,PEDS	1695	0.095
	BLOOD, R/O SBE	21	0.001
	C BLOOD	2935	0.164
	ISO BLOOD CULT	8	0.000
	LEPTO CULTURE,BLOOD	11	0.001
	MISC. C,BLOOD	1	0.000
	OTHER CULTURE,BLOOD	6	0.000
	PED BLOOD CULT	385	0.022
	PEDS BC	315	0.018
	SBE SUBCULTURE	409	0.023
	TRAN RX CUL,BLOOD	4	0.000
BLD CULT		133192	7.462
BLD PARA	BLOOD PARASITES	248	0.014
	MALARIA	74	0.004
	MALARIA SMEAR	156	0.009
	MICROFILARIA SP	1	0.000
BLD PARA		479	0.027
BORDETELLA CULT	B PERTUSSIS	23	0.001
	B. PERT	1	0.000
	BORDETELLA CULT	6	0.000
	BORDETELLA DFA	31	0.002

Laboratory test order classification

std_test_ord	tstorder	COUNT	PERCENT
BORDETELLA CULT	BORDETELLA SMEA	2	0.000
	BORDTELA S CULT	37	0.002
	PERTUS. CULT	9	0.001
	PERTUSS,FA	3	0.000
	PERTUSSIS	83	0.005
	PERTUSSIS CULT	34	0.002
BORDETELLA CULT		229	0.013
BRUCELLA CULT	BRUCELLA CULT	11	0.001
	C&S BRUCELL/TUL	2	0.000
BRUCELLA CULT		13	0.001
C DIFFICILE	C DIFF A+B	6	0.000
	C DIFFICILE	119	0.007
	C-DIFFICILE	54	0.003
	C. DIFFICILE	108	0.006
	C.DIFFICILE TOX	48	0.003
C DIFFICILE		335	0.019
CATH CULT	C CATH	19	0.001
	C&S IV CATH TIP	20	0.001
	CATH TIP	5	0.000
	CATH TIP C&S	3	0.000
	CATH TIP CULT	71	0.004
	CATHETER CULT	2	0.000
	CATHETER TIP	3	0.000
CATH CULT		123	0.007
CERVICAL CULT	CERV/STREP	2	0.000
	CERV/VAG	231	0.013
	CERVICAL CULTUR	54	0.003
CERVICAL CULT		287	0.016
CHLAMYDIA CULT	CHLAMYDIA CULT	252	0.014
	CHLAMYDIA PROBE	353	0.020
CHLAMYDIA CULT		605	0.034
CMV	CMV CULTURE	97	0.005
	CMV VR C/S	4	0.000
CMV		101	0.006
CSF CULTURE	ACANTHAMOEBA CU	30	0.002
	ANAEROBIC PANEL,CSF	3	0.000
	C CSF	753	0.042
	CSF	46	0.003
	CSF CUL/GRAM ST	63	0.004

Laboratory test order classification

std_test_ord	tstorder	COUNT	PERCENT
CSF CULTURE	CSF CULT	50	0.003
	CSF CULT-BNH	133	0.007
	CSF CULTURE	10196	0.571
	CSF PANEL	2135	0.120
	CSF SMEAR	5	0.000
	CSF VR PNL	38	0.002
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CSF CULTURE		13452	0.754
E COLI O157:H7	E COLI 0157:H7	2	0.000
	E COLI O157:H7	3	0.000
	E,COLI 0157:H7	67	0.004
	E.C. O157 CULT	12	0.001
	E.COLI 0157:H7	61	0.003
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E COLI O157:H7		145	0.008
EAR CULT	C EAR	113	0.006
	C&S EAR	167	0.009
	EAR C&S	261	0.015
	EAR CUL	97	0.005
	EAR CULT	817	0.046
	EAR CULTURE	38	0.002
	EAR CULTURE PAN	40	0.002
	EAR CX	33	0.002
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EAR CULT		1566	0.088
ENVIRON CULT BT	ENVIRO CULT	22	0.001
	ENVIRON CULT BT	421	0.024
	ENVIRON CULTURE	2	0.000
	ENVIRONMENT CUL	3	0.000
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ENVIRON CULT BT		448	0.025
EYE CULT	C EYE	288	0.016
	C&S EYE	460	0.026
	EYE C&S	255	0.014
	EYE CU	117	0.007
	EYE CULT	1222	0.068
	EYE CULTURE	225	0.013
	EYE CULTURE PAN	21	0.001
	EYE CX	74	0.004
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EYE CULT		2662	0.149
FECAL RS	FEC REDUCING SU	15	0.001
	FECAL RED SUBST	5	0.000
	RED SUB	1	0.000
	RED SUBST	2	0.000
	REDUCE STL	2	0.000
	REDUCING	17	0.001
	REDUCING SUBST	17	0.001

Laboratory test order classification

std_test_ord	tstorder	COUNT	PERCENT
FECAL RS	REDUCING SUBT	12	0.001
	STOOL RED SUBST	3	0.000
FECAL RS		74	0.004
FECAL WBC	FEC WBC	923	0.052
	FECAL LEUKOCYTE	1609	0.090
	FECAL WBC	1450	0.081
	FECAL WBCS	17	0.001
	FECALWBC	4	0.000
	STOOL WBC'S	206	0.012
	STOOLWBC	232	0.013
	WBC'S	45	0.003
FECAL WBC		4486	0.251
FOB	FOB	2157	0.121
	OC BLD	639	0.036
	OCC BL	4579	0.257
	OCC BLD	155	0.009
	OCC BLD X3	315	0.018
	OCC BLDX3	2848	0.160
	OCCBDX3	1242	0.070
	OCCBLDX3	184	0.010
	OCCULT	2329	0.130
	OCCULT BLOOD	28138	1.576
	OCCULT BLOOD X3	204	0.011
FOB		42790	2.397
FUNGUS, CSF	C FUNGAL,CSF	1	0.000
	CRYPTOCOCCUS AG,CSF	63	0.004
	FUNGAL CULT,CSF	31	0.002
	FUNGAL CULTURE,CSF	73	0.004
	FUNGAL MISC,CSF	54	0.003
	FUNGAL SMEAR,CSF	1	0.000
	FUNGAL,CSF	53	0.003
	FUNGI YEASTLIKE,CSF	1	0.000
	FUNGUS MICRO,CSF	1	0.000
	INDIA IN,CSF	1	0.000
	INDIA INK,CSF	41	0.002
	INDIA INK,CSF,CSF	1	0.000
	INDIA INK-CSF,CSF	9	0.001
	KOH PREP,CSF	1	0.000
	MYCOL C&SM,CSF	13	0.001
	MYCOLOGY CUL,CSF	3	0.000
	MYCOLOGY CULT,CSF	30	0.002
	MYCOLOGY,CSF	4	0.000
FUNGUS, CSF		381	0.021
FUNGUS, GENITAL	C FUNGAL,GEN	11	0.001
	FUNGAL CULT,GEN	80	0.004

Laboratory test order classification

std_test_ord	tstorder	COUNT	PERCENT
FUNGUS, GENITAL	FUNGAL CULT,GEN,GEN	5	0.000
	FUNGAL CULTURE,GEN	120	0.007
	FUNGAL CULTURE,GEN,GEN	12	0.001
	FUNGAL MISC,GEN	75	0.004
	FUNGAL MISC,GEN,GEN	6	0.000
	FUNGAL SMEAR,GEN	125	0.007
	FUNGAL,GEN	46	0.003
	FUNGAL,GEN,GEN	3	0.000
	FUNGAL-BNH,GEN	3	0.000
	FUNGI YEASTLIKE,GEN	24	0.001
	FUNGI YEASTLIKE,GEN,GEN	2	0.000
	FUNGUS ID,GEN	3	0.000
	KOH / WET PREP,GEN	108	0.006
	KOH / WET PREP,GEN,GEN	18	0.001
	KOH PREP,GEN	9526	0.534
	KOH PREP,GEN,GEN	744	0.042
	KOH,GEN	22941	1.285
	KOH,GEN,GEN	730	0.041
	KOH/NS,GEN	315	0.018
	KOH/NS,GEN,GEN	13	0.001
	KOH/WET PREP,GEN	772	0.043
	KOH/WET PREP,GEN,GEN	281	0.016
	MYCOL C&SM,GEN	4	0.000
	MYCOL C&SM,GEN,GEN	2	0.000
	MYCOLOGY CULT,GEN	80	0.004
	MYCOLOGY CULT,GEN,GEN	4	0.000
	MYCOLOGY SMEAR,GEN	4	0.000
	MYCOLOGY,GEN	15	0.001
	NS PREP,GEN	4570	0.256
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FUNGUS, GENITAL		40642	2.277
FUNGUS, OTHER	B/M CUL FUNGAL	1	0.000
	BLD CUL FUNGAL	7	0.000
	C FUNGAL	164	0.009
	DFA CRYPTO	34	0.002
	FUNG ID	19	0.001
	FUNGAL	3377	0.189
	FUNGAL BC	2	0.000
	FUNGAL BLD	5	0.000
	FUNGAL BLD CULT	25	0.001
	FUNGAL CUL	5791	0.324
	FUNGAL CUL/STN	8	0.000
	FUNGAL CULT	3388	0.190
	FUNGAL CULTURE	4921	0.276
	FUNGAL DERM	221	0.012
	FUNGAL MISC	1310	0.073
	FUNGAL SMEAR	343	0.019
	FUNGAL-BLOOD	3	0.000
	FUNGAL-BNH	45	0.003
	FUNGI FILAMENTO	22	0.001
	FUNGI YEASTLIKE	121	0.007
	FUNGUS ID	309	0.017

Laboratory test order classification

std_test_ord	tstorder	COUNT	PERCENT
FUNGUS, OTHER	FUNGUS MICRO	31	0.002
	KOH	3220	0.180
	KOH / WET PREP	10	0.001
	KOH PREP	1946	0.109
	KOH/NS	1	0.000
	KOH/WET PREP	2283	0.128
	MYCO CULT	2	0.000
	MYCOL C&SM	361	0.020
	MYCOLOGY	129	0.007
	MYCOLOGY CUL	93	0.005
	MYCOLOGY CULT	1399	0.078
	MYCOLOGY SMEAR	32	0.002
	NS PREP	24	0.001
	R/O DERMATOPHYT	1	0.000
	SALINE PREP,SKIN	10	0.001
	WET PREP,NAIL	143	0.008
	WET PREP,SCALP	30	0.002
	WET PREP,SKIN	217	0.012
FUNGUS, OTHER		30048	1.683
FUNGUS, RESP	C FUNGAL,RESP	32	0.002
	FUNG ID,RESP	4	0.000
	FUNGAL CULT,RESP	671	0.038
	FUNGAL CULTURE,RESP	562	0.031
	FUNGAL MISC,RESP	458	0.026
	FUNGAL SMEAR,RESP	12	0.001
	FUNGAL,RESP	285	0.016
	FUNGAL-BNH,RESP	1	0.000
	FUNGI FILAMENTO,RESP	21	0.001
	FUNGI YEASTLIKE,RESP	11	0.001
	FUNGUS ID,RESP	9	0.001
	FUNGUS MICRO,RESP	2	0.000
	KOH PREP,RESP	5	0.000
	MYCOL C&SM,RESP	8	0.000
	MYCOLOGY CULT,RESP	44	0.002
	MYCOLOGY,RESP	2	0.000
FUNGUS, RESP		2127	0.119
GC CULT/SMEAR/P	GC (DNA PROBE)	17	0.001
	GC CULT	64194	3.596
	GC CULTURE	14013	0.785
	GC CX	6	0.000
	GC PROBE	94	0.005
	GC SMEAR	10	0.001
	GC/CHL PROBE	40135	2.249
	GC/CHLAM	2791	0.156
	GC/CHLAM PROBE	9290	0.520
	GC/CHLAMYDIA PR	22380	1.254
	GC/CT PANEL	102	0.006
	GCSMEAR	3	0.000
	GISP	263	0.015

Laboratory test order classification

std_test_ord	tstorder	COUNT	PERCENT
GC CULT/SMEAR/P	N GONORRHOEAE	485	0.027
	R/O GC	114	0.006
GC CULT/SMEAR/P		153897	8.622
GENITAL CULTURE	AEROBIC CULT,GENITAL	24	0.001
	AEROBIC CULTURE,GENITAL	1	0.000
	ANAER CULT,GENITAL	5	0.000
	CULT & SENS,GENITAL	2	0.000
	CULTURE,GENITAL	2	0.000
	GENITAL CULTURE	27316	1.530
	MISC CUL,GENITAL	6	0.000
	MISCELLANEOUS,VAG CS	35	0.002
	OTHER CULTURE,GENITAL	3	0.000
	VAG CULT	67	0.004
	VAGINAL CULTURE	181	0.010
GENITAL CULTURE		27642	1.549
GIARDIA/CRYPTO	CRYPTOSPORI STN	15	0.001
	CRYPTOSPORIDIUM	53	0.003
	CRYPTOSPORIDUM=	1	0.000
	CRYSPOR	3	0.000
	GARDIA/CRYP DFA	12	0.001
	GIA & CRYPTO	14	0.001
	GIARD LAMB AG	62	0.003
	GIARDIA AG	40	0.002
	GIARDIA,DFA	65	0.004
	GIARDIA/CRYP SC	849	0.048
GIARDIA/CRYPTO		1114	0.062
GRAM STAIN	GM STAIN	1	0.000
	GRAM STAIN	10719	0.601
	GRAM STAIN SPEC	8	0.000
	GRAM STN	23	0.001
	GS & CULTURE	12	0.001
	GS AND CULTURE	41	0.002
GRAM STAIN		10804	0.605
GROUP A STREP	GRP A STREP CUL	3866	0.217
	R/O STREP	4549	0.255
	RAP STREP	658	0.037
	RAP STREP-KAHC	857	0.048
	RAPID STREP	28167	1.578
	RAPID STREP A	5858	0.328
	RAPSTP&C	397	0.022
	RPDSTP-C	191	0.011
	RS CONFIRM	6325	0.354
	STREP A PANEL	1230	0.069
	TC STREP	6088	0.341
GROUP A STREP		58186	3.260

Laboratory test order classification

std_test_ord	tstorder	COUNT	PERCENT
GROUP B STREP	B STREP A	16	0.001
	BETA STREP CUL	140	0.008
	BETASTRP	5	0.000
	C B STREP	2207	0.124
	C&S GBS OB/NEO	4850	0.272
	CERVICAL SCR-B	975	0.055
	CUL GBS VAG	1267	0.071
	GBBS	282	0.016
	GBS	1143	0.064
	GBS CULTURE	613	0.034
	GBS OB/GYN	1676	0.094
	GEN,ROBS	475	0.027
	GEN/STREP SCRN	408	0.023
	GP B BETA STREP	2500	0.140
	GP B ST	1861	0.104
	GP/B/CUL	1	0.000
	GPB CUL	1	0.000
	GROUP B CULTURE	196	0.011
	GROUP B SCR	718	0.040
	GROUP B SCREEN	1071	0.060
	GROUP B STREP	572	0.032
	GROUP B STREP.	28	0.002
	GRP B PEN_ALL	26	0.001
	GRP B STREP	2464	0.138
	GRP B STREP CUL	541	0.030
	OB PANEL X3	348	0.019
	OB/GYN STREP B	1992	0.112
	R/O BETA STREP	5771	0.323
	R/O GBS	4250	0.238
	R/O GP B STREP	3303	0.185
	R/O GRP B STREP	2373	0.133
	RECTAL GROUP B	340	0.019
	S AGALACTIAE ID	1964	0.110
	STREP AGAL CULT	141	0.008
	STREP B-HEMOLY	494	0.028
	STREP SCREEN NOT THR	1207	0.068
	VAG/REC GBS	802	0.045
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GROUP B STREP		47021	2.634
H DUCREYI CULT	H DUCREYI CULT	8	0.000
H PYLORI CULT	CLO	1	0.000
	CLO TEST	668	0.037
	H PYLORI CULTUR	204	0.011
	H.PYLORI	15	0.001
	HELICOBACTER P	976	0.055
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H PYLORI CULT		1864	0.104
HERPES	HER DFA	1	0.000
	HERPES CULT	4444	0.249
	HERPES CULTURE	353	0.020

Laboratory test order classification

std_test_ord	tstorder	COUNT	PERCENT
HERPES	HSV CULT/AG	1	0.000
	HSV CULTURE	142	0.008
	HSV DFA	160	0.009
	OB HERPES CULT	4	0.000
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HERPES		5105	0.286
INFLUENZA	FLU A PANEL	608	0.034
	INFLU SURVEY	337	0.019
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INFLUENZA		945	0.053
LEGIONELLA CUL	LDFA	3	0.000
	LEGIONELLA CUL	31	0.002
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LEGIONELLA CUL		34	0.002
LEISHMANIASIS	LEISHMANIASIS	151	0.008
MICROORG ID	MICROORG ID	33	0.002
MISC CULTURE	BIO C&S	1	0.000
	BIOPSY CULT	2	0.000
	BODYSITE CULT	1	0.000
	BR BRUSH C&S	8	0.000
	BR LAVAGE C&S	48	0.003
	BRONCH CULTURE	34	0.002
	BSGB CX	7	0.000
	C IUD	12	0.001
	C&S GASTRIC ASP	4	0.000
	C&S MOUTH	22	0.001
	C&S SKIN	856	0.048
	CF CULTURE	80	0.004
	CULT & SENS	66	0.004
	CULT,MISC	11	0.001
	CULT,OTHER	9	0.001
	CULTURE	455	0.025
	CULTURE, OTHER	14	0.001
	CX, SURGICAL	15	0.001
	DRAIN/CYST CX	40	0.002
	IUD	1	0.000
	JOINT C&S	8	0.000
	LEPTO CULTURE	2	0.000
	MED DEVICE CX	1	0.000
	MISC CS	27	0.002
	MISC CUL	118	0.007
	MISC CULT	8	0.000
	MISC CULTURE	648	0.036
	MISC CX	266	0.015
	MISC. C	1	0.000
	MISCELLAN. CX	20	0.001
	MUMPS CULTURE	1	0.000
	OTHER CULTURE	391	0.022

Laboratory test order classification

std_test_ord	tstorder	COUNT	PERCENT
MISC CULTURE	RECT CX	2	0.000
	SM CULT	8	0.000
	SURF C&S	6	0.000
MISC CULTURE		3193	0.179
MRSA	MRSA	43	0.002
	MRSA CULTURE	13	0.001
	R/O MRSA	1117	0.063
	STAPH ID	13	0.001
MRSA		1186	0.066
MYCOPLASMA CULT	M PNEUMO CULT	1	0.000
	MYCOPLASA ID	2	0.000
	MYCOPLASMA CULT	5	0.000
MYCOPLASMA CULT		8	0.000
NASAL CULT	AER CULT,NASAL	1	0.000
	AEROBIC CULT,NASAL	721	0.040
	AEROBIC CULT,THROAT,NASAL	16	0.001
	AEROBIC CULT,THROAT,NASAL,NASAL	7	0.000
	AEROBIC CULTURE,NASAL	28	0.002
	ANAER CULT,NASAL	24	0.001
	ANAEROBE-APATH,NASAL	10	0.001
	ANAEROBIC PANEL,NASAL	70	0.004
	C NASAL/SINUS	132	0.007
	CULTURE,NASAL	11	0.001
	CULTURE,THROAT,NASAL	2	0.000
	MISC CULTURE,NASAL	7	0.000
	MISC CX,NASAL	24	0.001
	MISC. C,NASAL	1	0.000
	N-P CULTURE	1	0.000
	NASAL	12	0.001
	NASAL CULT	1562	0.088
	NASAL CULTURE	1173	0.066
	NASAL CX	7	0.000
	NASO-PHAR CULT	4	0.000
	NOSE CULTURE	6	0.000
	NP	14	0.001
	NP CULTURE	45	0.003
	OTHER CULTURE,NASAL	80	0.004
NASAL CULT		3958	0.222
O & P	DIRECT O&P EXAM	1	0.000
	INTESTINAL PARA	219	0.012
	O & P	12	0.001
	O&P	980	0.055
	O&P CONCENTRATE	48	0.003
	O&P EXAM	2370	0.133
	O&P EXM	181	0.010

Laboratory test order classification

std_test_ord	tstorder	COUNT	PERCENT
O & P	O&P ID	1858	0.104
	O&P MACRO	5	0.000
	O&P MICR	33	0.002
	O&P PANEL	684	0.038
	O&P/TRICHROME	3	0.000
	O+P EXAM	676	0.038
	OOCYST EXAM	8	0.000
	OP DIRECT	120	0.007
	OP EXAM	158	0.009
	OP MACRO	4	0.000
	OP TRICHROME	269	0.015
	OVA & PARA	412	0.023
	OVA & PARASITE	528	0.030
	OVA & PARASITES	2549	0.143
	OVA&PAR	345	0.019
	PARASITE EXAM	13	0.001
	PARASITE TEST	511	0.029
	SP O&P	10	0.001
	SPUTUM PARASITE	2	0.000
	TRICHROME STAIN	14	0.001
O & P		12013	0.673
ORGANISM ID	ECTOPARASITE	5	0.000
	ORGANISM ID	116	0.006
	VECTOR ID	4	0.000
ORGANISM ID		125	0.007
OTHER	BACT ANTIGENS	77	0.004
	BF:CRYSTAL EXAM	1	0.000
	CLINTEST	19	0.001
	FRUCTOSE	14	0.001
	GROSS BLOOD	3	0.000
	GROSS BLOOD.	4	0.000
	LATEX PANEL	31	0.002
	MACRO	10	0.001
	MISC STAIN	1	0.000
	MISCELLANEOUS	383	0.021
	PH,STOOL	8	0.000
	PRES OF SPERM	147	0.008
	RDSP	62	0.003
	RECTAL	7	0.000
	REFERRED ID/SEN	246	0.014
	SEL BACT AGENT	40	0.002
	SEMEN PROFILE	224	0.013
	STOOL PH	120	0.007
	STOOL/PH	3	0.000
	STREP OTHER	10	0.001
	WELLCOGEN TEST	32	0.002
OTHER		1442	0.081

Laboratory test order classification

std_test_ord	tstorder	COUNT	PERCENT
OTHER GI	FAT,MICROSCOPIC	91	0.005
	FEC MACRO EXAM	15	0.001
	FECAL EXAM	42	0.002
	FECAL FAT	51	0.003
	FECAL FAT,QUAL	126	0.007
	GASTRIC	4	0.000
	MACRO EXAM STOO	13	0.001
	OCC BLD-GASTRIC	14	0.001
	QUAL FECAL	39	0.002
	QUAL FECAL FAT	17	0.001
	STOOL	16	0.001
	STOOL FECAL FAT	35	0.002
	STOOL GR EXAM	423	0.024
OTHER GI		886	0.050
OTHER STD	C&S GENITAL-TM	10574	0.592
	DARKFLD	1	0.000
	HPV	5	0.000
	HPV PROFILE	1	0.000
	INP CHLAMYDIA	15	0.001
	SALINE MOUNT	8	0.000
	SALINE PREP	1693	0.095
	UREAPLASMA ID	1	0.000
	URETHRAL C&S	7	0.000
	URETHRAL CULTUR	3	0.000
	W-PREP	4	0.000
	WET PREP	47913	2.684
	WET PREP NS	6	0.000
	WET PREP SALINE	12	0.001
OTHER STD		60243	3.375
PAP SMEAR	PAP	436	0.024
	PAP(TRICARE)	397	0.022
PAP SMEAR		833	0.047
PINWORM	MICRO PIN WORM	97	0.005
	PIN WORM EXAM	46	0.003
	PINWORM	439	0.025
	PINWORM EXAM	34	0.002
	PINWORM PREP	177	0.010
	WORM ID	16	0.001
PINWORM		809	0.045
RECTAL CULT	RECTAL CULT	9	0.001
	RECTAL CULTURE	5	0.000
RECTAL CULT		14	0.001
RESP CULT	CULTURE RESPIRA	28	0.002

Laboratory test order classification

std_test_ord	tstorder	COUNT	PERCENT
RESP CULT	LOW RESP CULT	48	0.003
	LOWER RESP CULT	91	0.005
	RESP CULT	4735	0.265
	RESP PANEL	368	0.021
	RESP. CULTURE	68	0.004
	UPPER RESP CUL	65	0.004
	UPPER RESP CULT	1	0.000
RESP CULT		5404	0.303
RESP CULTURE	AEROBIC CULT,RESP	56	0.003
	CULT & SENS,RESP	12	0.001
RESP CULTURE		68	0.004
ROTAVIRUS	ROTAVIRUS	35	0.002
RSV	RSV	470	0.026
	RSV SCREEN	212	0.012
	RSV TEST	194	0.011
RSV		876	0.049
SKIN CULT	AEROBIC CULT,NASAL,SKIN	1	0.000
	AEROBIC CULTURE,NASAL,SKIN	1	0.000
	SKIN C&S	71	0.004
	SKIN CULTURE	122	0.007
	SKIN CX	35	0.002
SKIN CULT		230	0.013
SPUTUM CULT	AEROBIC CULT,SPUTUM	22	0.001
	AEROBIC CULTURE,SPUTUM	14	0.001
	ANAER CULT,SPUTUM	1	0.000
	ANAEROBIC PANEL,SPUTUM	7	0.000
	C SPUTUM	614	0.034
	C&S SPUTUM	587	0.033
	CF CULTURE,SPUTUM	142	0.008
	SP C&S	1	0.000
	SPU CULT	71	0.004
	SPUT C&S/SMEAR	94	0.005
	SPUTUM C	1	0.000
	SPUTUM C&S	184	0.010
	SPUTUM C&S/GRAM	175	0.010
	SPUTUM CU	24	0.001
	SPUTUM CULT	519	0.029
	SPUTUM CULTURE	760	0.043
	SPUTUM CX	19	0.001
	SPUTUM PANEL	80	0.004
	SPUTUMCX	22	0.001
SPUTUM CULT		3337	0.187

Laboratory test order classification

std_test_ord	tstorder	COUNT	PERCENT
SSC	CAMPY CULTURE	1	0.000
	CAMPY ID	8	0.000
	CAMPYLOBACTER	133	0.007
	S/S SCREEN	32	0.002
	SALMONELLA GRP	1	0.000
	SHIGELLA SERO	5	0.000
	STOOL,SALM/SHIG	20	0.001
	STOOL:SSC	13	0.001
	STOOL:SSCE	125	0.007
	STOOL:SSE	6	0.000
SSC		344	0.019
STOOL CULT	AEROBIC CULT,STOOL	156	0.009
	C STOOL	2	0.000
	CULTURE,STOOL	1	0.000
	STOOL CUL	1	0.000
	STOOL CULT	26376	1.478
	STOOL CULTURE	824	0.046
	STOOL CX	563	0.032
STOOL CULT		27923	1.564
THR CULT	AEROBIC CULT,THROAT	54	0.003
	AEROBIC CULTURE,THROAT	1	0.000
	ANAER CULT,THROAT	32	0.002
	ANAEROBIC CULT,THROAT	2	0.000
	CULTURE,THROAT	3	0.000
	MISC CULTURE,THROAT	9	0.001
	MISC CX,THROAT	4	0.000
	OTHER CULTURE,THROAT	1	0.000
	PROJECT GARGLE	312	0.017
	TC	3811	0.214
	TC OTHER	39	0.002
	TC SCREEN	1111	0.062
	THR CULT	413984	23.193
	THROAT	3187	0.179
	THROAT CULTURE	29830	1.671
THR CULT		452380	25.344
TISSUE CULT	BIOPSY	23	0.001
	C TISSUE	57	0.003
	C&S TISSUE/BONE	42	0.002
	TISSUE BK CX	1	0.000
	TISSUE C&S	40	0.002
	TISSUE CULT	113	0.006
	TISSUE CULTURE	636	0.036
TISSUE CULT		912	0.051
UA CULT	AEROBIC CULT,URINE	5	0.000
	ANAER CULT,URINE	1	0.000

Laboratory test order classification

std_test_ord	tstorder	COUNT	PERCENT
UA CULT	LEPTO CULTURE,URINE	10	0.001
	OB UA	190	0.011
	UA CULT	505027	28.293
	UA MICRO SCREEN	2804	0.157
	UA PEDS	1223	0.069
	UC	511	0.029
	UR CULT	7529	0.422
	UR CULT LOW	1	0.000
	UR CULT,LOW	1	0.000
	URINE CULT-BNH	8438	0.473
	URINE CULTURE	1616	0.091
	URINE CX	3284	0.184
UA CULT		530640	29.728
VARICELLA	V ZOSTER CULT	2	0.000
	VARICEL CULT	105	0.006
	VZ-DFA	2	0.000
	VZV CULTURE	12	0.001
	VZV DFA	12	0.001
VARICELLA		133	0.007
VIBRIO	VIB-AER	19	0.001
	VIB/YER/E0157	206	0.012
	VIBRIO	2	0.000
	VIBRIO SP IDENT	1	0.000
VIBRIO		228	0.013
VIRAL CULT	ENTEROVIRUS CUL	8	0.000
	RESP VIRUS CULT	438	0.025
	VIRAL CULT	1959	0.110
	VIRAL CULTURE	349	0.020
	VIRAL CX	6	0.000
	VIRUS ID	251	0.014
VIRAL CULT		3011	0.169
VIRAL PANEL	VIRAL PNL	19	0.001
VRE	R/O VRE	4	0.000
WND CULT	ABSCESS CULTURE	287	0.016
	AER WOUND/GRAM	93	0.005
	AEROBIC CULT,WND	652	0.037
	ANA WOUND/GRAM	3	0.000
	ANAER CULT,WND	70	0.004
	ANAEROBE-APATH,WND	5	0.000
	ANAEROBIC PANEL,WND	38	0.002
	C&S WOUND	2	0.000
	CULTURE,WOUND	294	0.016
	LESION CX	11	0.001

Laboratory test order classification

std_test_ord	tstorder	COUNT	PERCENT
WND CULT	WAR WOUND	112	0.006
	WND CULT	30696	1.720
	WOUND ANA-BNH	276	0.015
	WOUND CULTURE	3817	0.214
	WOUND CX	148	0.008
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WND CULT		36504	2.045
YERSINIA CULT	YER.CUL	32	0.002
	YER/VIB	35	0.002
	YERSIN	8	0.000
	YERSINIA CULT	3	0.000
	YERSINIA CULTUR	88	0.005
	YERSINIA SP ID	1	0.000
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YERSINIA CULT		167	0.009
		=======	=======
		1784959	100.000

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